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A CASE OF HYDROCEPHALUS IN AN INFANT, WITH COMMENTS ON THE SECRETION, CIRCULATION AND ABSORPTION OF THE CEREBRO-SPINAL FLUID

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(*Continued from page* 384)

The Tissue-fluid of the Brain and Spinal Cord

A FACTOR of primary importance in connection with the production of hydrocephalus, and the administration of drugs in affections of the central nervous system, is the relationship between the perineuronal fluid and the fluid of the sub-arachnoid space. The problem is to decide whether (1) the fluid which is contained in the perineuronal spaces is to be regarded as a tissue-fluid or "lymph" which is confined in the nerve tissue, or (2) whether there is direct continuity between this fluid and the cerebro-spinal fluid contained in the meshes of the arachnoid membrane.

As is well known, the larger cortical vessels which penetrate the brain substance, at right angles to its surface, are accompanied for a variable distance by a membranous sheath derived from the pia-arachnoid. This is known as the perivascular sheath. Between it and the wall of the arteriole or venule is a space traversed by fine trabeculae, which contains cerebro-spinal fluid. This, the perivascular space (see fig. 11) is continuous externally with the sub-arachnoid space. The cellular lining of the perivascular sheath is generally spoken of as mesothelial, and as being derived from the mesoblast.

A few authors, however, have regarded both sub-arachnoid endothelium and its perivascular prolongations into the neural substance as epiblastic in origin, through the medium of the neural crest. This is an important conception to which further reference will be made later.

The perivascular sheath has been believed by some authors to form an uninterrupted semi-permeable or even impermeable membrane, which, like the arachnoid, is capable of limiting the cerebro-spinal fluid, and probably of permitting passage of it in one direction only. The general mesothelium of the sub-arachnoid space has been supposed by many to isolate the cerebro-spinal fluid so completely as to prevent any addition to it, quantitative or qualitative, or subtraction from it by the meningeal blood vessels. French authors have even spoken of this endothelium as functioning as a sort of varnish, rendering

the sub-arachnoid space, as it were, waterproof. Many even of the larger sub-arachnoid venules are so thin-walled, however, that it is difficult to believe that they take no part in the disposal of the adjacent fluid.

External to the perivascular sheath, and forming the immediate covering of the surrounding brain substance, is an outer sheath which, if traced outwards towards the surface, is seen to be continuous with the external limiting membrane covering the surface of the brain. Since this membrane is obviously a condensation of the neuroglia tissue, it may be regarded as epiblastic in

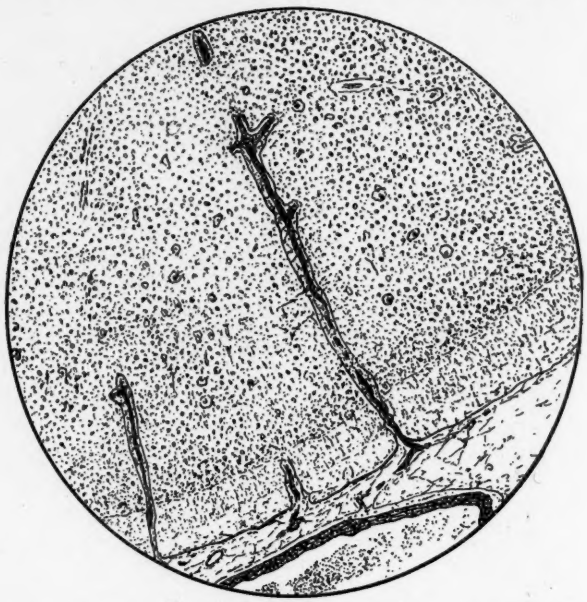

Fig. 11. Coronal section through the cortex cerebri close to the superior longitudinal sinus. Part of a large superficial cerebral vein is seen in the pia arachnoid tissue; also a cortical vessel surrounded by its perivascular sheath. Capillary vessels are seen cut at various angles in the adjacent cortex, each of which is surrounded by a pericapillary sheath.

origin, and may be termed the glial sheath. Many of the smaller vessels and capillaries entering the cortex are surrounded by the glial sheath only, and their walls are thus in direct contact with the nerve tissue and the fluid within its spaces.

If the larger cortical vessels are traced inwards the perivascular sheath appears to blend on its superficial aspect with the glial sheath, and on its deep or inner surface with the adventitia of the vessel wall. Thus the perivascular space which is continuous externally with the sub-arachnoid space is believed by some authors to end internally in a sort of *cul de sac* near the situation in which the arteriole or venule becomes continuous with the

capillaries in the brain substance. In some places, however, the perivascular spaces seem to be continuous with the "pericapillary" spaces which surround the smaller capillaries of the brain or cord, and so with the meshes of the neuro-reticulum, and the spaces which surround some of the larger neuroglia cells and nerve cells (fig. 12). This appearance is regarded by some writers as due to shrinkage of the nerve tissue. The pericapillary and perineuronal spaces are, however, present in well-fixed preparations, in which there is little evidence of shrinkage in other situations, and in which the preservation, without rupture,

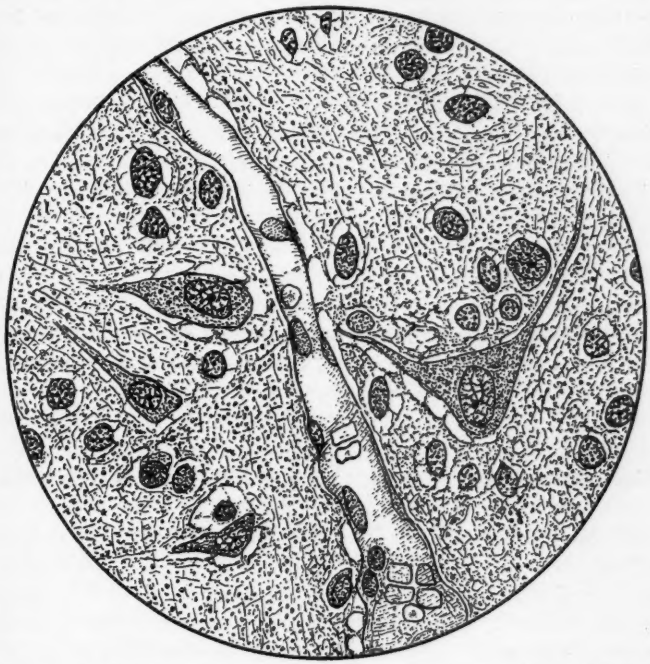

Fig. 12. Drawing, under an oil immersion lens, of a capillary vessel and cortical cells, showing the communication of perineuronal spaces with pericapillary spaces, from the same specimen as the preceding figure.

of the exceedingly delicate trabeculae which cross the space, may be regarded as additional witness of the existence of both perineuronal and pericapillary spaces in the living tissue.

In some situations the endothelial wall of the smaller vessels appears to be in direct contact, or even continuity with the surrounding neuroglia without any intervening space; while in others a considerable space is present. It is possible therefore in the latter for osmosis or transudation to occur, either from capillary to space or from space to capillary. On the available

evidence we are inclined to believe that the *cul de sac* referred to by many observers is apparent rather than real, and that there is, through the medium of the perivascular canals, continuity between the tissue juices of the central nervous system and the sub-arachnoid fluid.

The importance of this relation, and of the source of the perivascular liquid, will become apparent when these are considered in connection with:

(1) The possibility of a direct absorption of the cerebro-spinal fluid into the capillaries of the brain and spinal cord. This is believed by certain authors to be the normal route by which absorption takes place; others, however, consider that absorption occurs in this way only under conditions in which the normal outflow becomes reversed by a considerable rise in the pressure of the sub-arachnoid fluid.

(2) The excretion of waste products of the brain's activity, either by absorption from the perineuronal fluid directly into the capillaries and venules, or by an outward flow of the tissue fluid from the perineuronal spaces, through the pericapillary and perivascular channels into the sub-arachnoid space, there to mingle with the cerebro-spinal fluid.

(3) The route by which absorption occurs of certain drugs when introduced directly into the sub-arachnoid cavity, by cistern- or lumbar-puncture, e.g. salvarsanised serum.

(4) The action of drugs administered by the mouth or intravenously, which are said to be eliminated in the cerebro-spinal fluid, e.g. urotropine. This drug has been employed in suppurative meningitis in the hope that it can exert a direct antiseptic action on the membranes; but it would seem that the normally alkaline cerebro-spinal fluid would need to attain a degree of acidity incompatible with life, before such an action could occur, since urotropine acts only in an acid medium.

(5) The mode of action of certain bacterial toxins such as that of tetanus.

The toxin of tetanus is generally believed to reach the central nervous system by passing along the perineural lymphatics[1]. Since these lymphatics communicate with the sub-arachnoid space, it would appear that the final stage of its journey would lie through the cerebro-spinal fluid, first in the sub-arachnoid space, and then in the perivascular canals; where according to the experimental evidence it would probably meet with a contrary, although extremely sluggish, stream. Presumably the toxin is absorbed into the central nervous system, partly directly from the wound *via* the lymph-clefts of the nerves supplying the injured area which the tetanus bacillus infects, and partly by the lymphatics in the nerves of the body generally, in the end-organs of which the poison has been deposited by the blood stream: for intravenous injections of tetanus toxin result after a certain latent period in generalised convulsions.

[1] Experiments in which removal of the perineural sheath is attempted, with a view to showing that the toxin is carried entirely by axis-cylinders, are inconclusive, since the operation is technically very difficult and does not in any case remove the lymph-channels in the endoneurium.

In view, however, of the extensive circulation of the cerebro-spinal fluid, it seems quite possible that spread of the disease through the cord is in part brought about by dissemination of the toxin in its currents or by diffusion. The increased toxicity of tetanus toxin when administered directly to the cerebro-spinal fluid[1] thus finds a ready explanation. While mineral and alkaloidal poisons, administered by the mouth or by the veins achieve their results in the nervous system by passing through the walls of the cerebro-spinal capillaries—the epithelium of the choroid plexuses preventing direct passage into the cerebro-spinal fluid—it is not surprising that when introduced into the sub-arachnoid space, they reach the neural elements in greater concentration, and thus bring about swifter and more dire results. Nevertheless, it is to be borne in mind that the major portion of any substance injected into the sub-arachnoid cavity is absorbed into the venous system without traversing the cerebral capillaries at all, in spite of manifestations of increased toxicity when so injected. Hence it is difficult to believe that salvarsanised and other sera when introduced into the theca can reach their intended destination in effective therapeutic concentration. For the salvarsan is entangled with the large molecules of the serum proteins which could diffuse but ineffectually against the outgoing perivascular currents, as compared with the smaller and more easily diffusible molecules of a bacterial or mineral poison. We conclude therefore that the serum is again absorbed into the blood stream from which it was originally abstracted. Moreover, the perivascular spaces at the surface of a syphilitic lesion are encumbered and blocked with cellular exudation, so that the regions in which active disease is progressing are not easily reached.

There are thus two questions to be considered, both of which are of fundamental importance: (1) Is there a continuity between the perivascular spaces on the one hand, and the pericapillary and perineuronal spaces of the brain and spinal cord on the other? (2) What is the normal direction of the current of fluid in the perivascular spaces? The answer to the latter question will, in addition, settle the problem of the origin of the perivascular liquid, i.e. whether it is cerebro-spinal fluid in the proper sense of the term, or whether it is derived from the pericapillary fluid, and so resembles lymph.

With reference to the first question, about which there has been considerable controversy, a careful examination of a large number of sections of the normal brain and cord has led us to the belief that a continuity or virtual passage exists between some, if not all, of the pericapillary and perivascular spaces, but that in normal circumstances it is not a very free communication. In pathological conditions in which there is shrinkage of the tissues, e.g. "hydrocephalus *ex vacuo*," there is a wide and free communication.

The second question admits of three possible replies. The normal current may be set in an outward direction, or in an inward direction; or there may be an ebb and flow of fluid, inwards at one time, and in the contrary direction at others, according to circumstance.

[1] Roux and Borrel (quoted by Weed(33)).

In attempting to solve this problem, some help is obtained from a consideration of the differences which exist between the ventricular and sub-arachnoid fluids. Cushing (4), quoting Jacobson, states that the ventricular fluid differs slightly from the sub-arachnoid fluid. Thus there is a higher percentage of sugar in the ventricular as compared with the sub-arachnoid liquid, but a lower concentration of albumen. These differences are generally interpreted as resulting from an addition of perivascular fluid to the true choroidal secretion which has passed from the ventricles into the sub-arachnoid space. A "dual source" (Weed (33)) of the cerebro-spinal fluid has thus been assumed, viz. (1) the choroidal secretion, and (2) a transudate from the cerebral capillaries. Strong evidence in favour of this view was afforded by Weed's experiments. He injected, at pressures only slightly above the normal, an isotonic solution capable of depositing granules of Prussian blue on fixation with acidified formalin. Post-mortem, the granular material was found in the sub-arachnoid space into which the solution had been introduced, and also in the arachnoidal villi. No granules, however, were discoverable in the perivascular spaces. Only when these spaces were enlarged by bleeding from the carotid artery and jugular vein before death, were blue granules seen in this situation. These experiments strongly suggested that the current in the perivascular spaces usually pursues an outward course, but since it is capable of experimental reversal, such reversal can occur in nature. A similar conclusion might be reached from a consideration of the behaviour of cells effused in inflammatory diseases of the brain. In encephalitis lethargica and cerebral syphilis, lymphocytes and plasma cells are found both in the sub-arachnoid fluid and in the spaces around the vessels, and presumably reach the former from the latter. Mere mechanical pushing out of cells by newly added cells hardly seems to account for the process; it would seem as if the outward trend of the perivascular liquid was, at least in part, responsible. In sub-arachnoid bleeding, on the contrary, the red blood corpuscles have been observed to pass inwards into these spaces.

Absorption of the Cerebro-spinal Fluid

Weed's well-known experiments, referred to above, of injecting the sub-arachnoid spaces at a low pressure with an isotonic solution of iron ammonium citrate and potassium ferrocyanide have shown that the granules of Prussian blue, which were subsequently precipitated in the tissues by the action of hydrochloric acid, are constantly found in certain situations. These situations, which may be taken as representing pathways of absorption of the fluid, include, in addition to the sub-arachnoid space in which the unabsorbed remnant is seen, the meshes of the arachnoidal villi and Pacchionian bodies. The granules are also found in the mesothelial cells forming the caps on the villi and Pacchionian bodies, and in the arachnoidal cell-nests in the dura mater. Weed did not find any large number of granules in the cerebral veins, although they were abundant in the intracranial venous sinuses, and he thus

came to the conclusion that the principal channel for the absorption of the cerebro-spinal fluid was through the arachnoidal villi into the venous sinuses. Weed considered that the cerebral veins are not normally concerned in absorbing the fluid, and in support of this conclusion he gave the following reasons: (1) the absence of a capillary bed in the pia mater; (2) the paucity of Prussian blue granules found in these veins in his injection experiments. Although in a general sense the former statement is correct, it is liable to give rise to a serious misconception, viz. that there are no capillary vessels in the

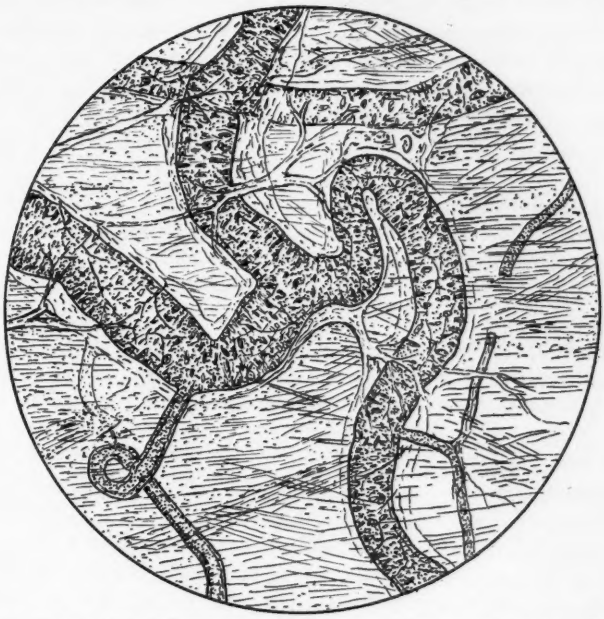

Fig. 13. Vessels of the human pia arachnoid. From a film preparation stained with haematoxylin and eosin.

pia mater, and that therefore it is impossible for absorption of cerebro-spinal fluid to take place into the veins of the pia covering the surface of the brain and spinal cord. Capillary vessels are, however, abundant in the pia arachnoid of both brain and spinal cord. Their presence may be easily demonstrated by either film preparations of the pia arachnoid (figs. 13 and 14), or sections of the central nervous system in which the membranes have been preserved intact. The peculiarity of the blood circulation here consists in the fact that a large number of small thin-walled arterioles and capillaries pass directly into the nervous substance, where they break up into a capillary plexus from which small venules and capillaries return the blood to the veins of the pia mater. The larger vessels are accompanied by a perivascular and neuroglial sheath,

the capillary vessels by a glial sheath only. Thus, although capillary plexuses are situated in the substance of the brain and spinal cord, there are capillary vessels in the pia mater, and also thin-walled venules, the walls of which consist of little more than the endothelial lining of the vessel. Cerebro-spinal fluid could therefore reach the cerebral veins by way of the capillaries and venules in the pia, instead of by the more circuitous route of the perivascular spaces and cerebral capillaries. This was the view entertained by Dandy and Blackfan (7), and merits careful consideration.

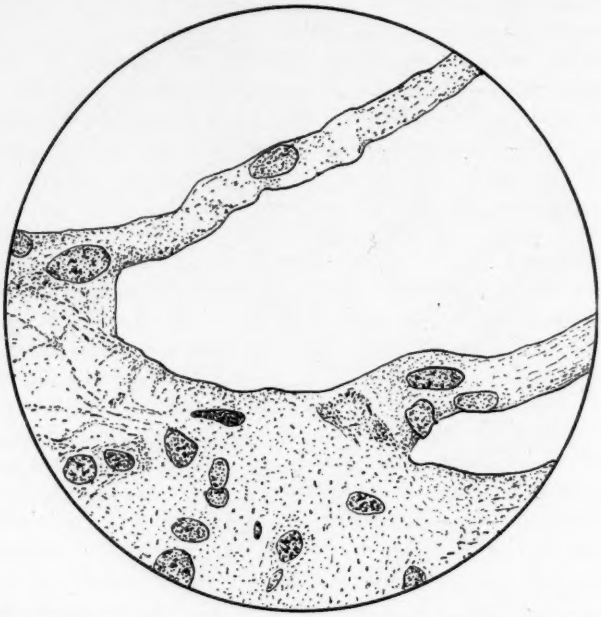

Fig. 14. Capillary vessels entering a venule. From the film preparation shown in fig. 13. Only the vessels are shown.

All authors are agreed that the lymphatic pathway is an accessory channel of absorption of the cerebro-spinal fluid. Many, following the pioneer work of Key and Retzius, in this as in other directions, have injected the perineural lymphatics and so the adjoining lymphatic glands by introducing various substances into the sub-arachnoid space. The sub-arachnoid space has likewise itself been injected from the perineural lymphatics. These experiments, as Weed pointed out (33), had the disadvantage of being conducted under various abnormal conditions; viz. in the living animal under anomalously high injection-pressures, or using suspensions of solid particles rather than true solutions capable of depositing coloured substances on suitable fixation; or else in the dead body. They thus gave inadequate evidence as to the direction

of flow during life. Weed (33), using his ferrocyanide method, found that the solution passed outwards along the perineural lymphatics when introduced into the sub-arachnoid space. In addition to the general perineural lymphatics, and their adjacent glands, the episcleral space and the nasal mucosa were injected. The communication between the episcleral space, morphologically an epidural space, and the space around the central fibres of the optic nerve, which is a continuation of the sub-arachnoid space, is worthy of further study. In addition, the granular precipitate was found in the nasal mucosa, where it occurred in lymphatic vessels; the solution had apparently reached the nose by passing down the olfactory nerves. In order to reach these lymphatics, or in the case of the spinal nerves, the lymph vessels leading to the neighbouring glands, it seemed to Weed that the injection material, after reaching the nerve or the nasal mucosa from the perineural lymphatics, lay at first free in the tissue spaces; and that it had to traverse these spaces before attaining the efferent channels in question.

In spite of the extent of the lymphatic vessels which lead from the sub-arachnoid space outwards along the nerves, it would seem that, quantitatively at least, only a minor portion of the cerebro-spinal fluid escapes by them. This has been shown by many investigators. Thus Lewandowsky (quoted by Weed and others) found that potassium ferrocyanide, injected into the cerebro-spinal fluid appeared much earlier and in far greater abundance in the blood of the internal jugular vein than in the lymph of the thoracic duct, while Dandy and Blackfan (7) obtained similar results using phenolsulphonephthalein.

Weed found that villi are absent from the spinal part of the arachnoid membrane, and concluded that such absorption as occurs there must be mainly lymphatic. In support of this view he found that phenolsulphonephthalein, when introduced into the lumbar sub-arachnoid cavity, appeared freely in the urine after a short space of time, only if the normal wide communication between the cranial and lumbar sub-arachnoid spaces were preserved. If this communication was closed artificially, as by ligaturing the membranes in the cervical region, absorption of the dye from the isolated spinal arachnoid was slow and scanty, and occurred only after a considerable latent period, as indicated by the output in the urine. Special care was taken to avoid compressing the cord by the ligature, so that no fall of arterial blood pressure, which would have vitiated the results, took place (33). These experiments would seem to localise the absorption of the cerebro-spinal fluid to the vault of the skull, where the arachnoidal villi are abundant. Keith has laid stress on the absence of convolutionary imprints in this region, as indicating that there is a thicker layer of fluid here than elsewhere over the convexity of the hemispheres; this condition, while partly at least due to gravity, may be in some way connected with the passage of the cerebro-spinal fluid into the veins in this area. The occurrence of that type of obstructive hydrocephalus described by Dandy and Blackfan (7) under the title of "communicating," which is due to adhesions around the mid-brain occluding the *incisura tentorii* and

preventing the upward diffusion of the cerebro-spinal fluid, is to some extent in favour of Weed's hypothesis. Dandy and Blackfan were able to induce this condition experimentally by introducing strips of gauze soaked in iodine around the mid-brain. These authors, however, found that phenolsulphonephthalein was absorbed from the isolated spinal sub-arachnoid space proportionately as quickly and as abundantly as from the same space when in free normal communication with its cranial continuation. This is a point of great importance; for while Weed's results appear to substantiate his claims for the arachnoidal villi as the main channels of escape for the cerebro-spinal fluid, the results of Dandy and Blackfan's experiments would seen to diminish their importance.

Mainly as a result of these experiments, Dandy and Blackfan came to the conclusion that the cerebro-spinal fluid is absorbed into the capillaries of the pia arachnoid. Although the capillary blood pressure is admittedly higher than the pressure of the sub-arachnoid fluid (240 mm. of water as compared with 100 mm. of water), it is by no means easy to disprove this theory, for there is no lack of thin-walled vessels in the pia mater (fig. 14). It may well be that there are three channels of escape for the watery liquid of the sub-arachnoid spaces: (1) the arachnoidal villi and their enlargements, the Pacchionian bodies; (2) the perineural lymphatics; and (3) the thin-walled vessels —capillaries and venules—of the leptomeninges. With reference to the third of these possibilities, it is to be remembered that although the capillary pressure is higher than the sub-arachnoid pressure, the reverse is probably true of the venules, and, moreover, osmotic influences might play a part. It might be objected that cerebro-spinal fluid is isotonic with blood. The fluid is, however, scanty in proteins, as compared with blood plasma; and, as Starling has shown, the proteins of plasma are capable of exerting a definite, if small, osmotic pressure which would have to be taken into account.

In cases of hydrocephalus *ex vacuo*, the ependyma is frequently seen to be shed from small areas of the ventricular wall, thus making it possible for a percolation of fluid to take place from the ventricles into the tissue spaces of the brain or in the contrary direction. We regard the ependyma as controlling and limiting ventricular absorption of cerebro-spinal fluid. It seems possible that if the ependyma is diseased, as in old age, the bulk of the hydrocephalus *ex vacuo* will be ventricular, but should the ependyma remain intact, the hydrocephalus will be mainly external and subarachnoid rather than subdural.

In this connection the ventricular absorption of cerebro-spinal fluid is of importance in the development of hydrocephalus. Extreme grades of dilatation of the ventricles, such as are often met with, would be hardly possible in the absence of some ventricular absorption; the choroid plexus would fail, and cease to secrete behind an absolute obstruction just as the kidney atrophies when the ureter is suddenly and completely blocked. While in some cases the obstruction at the foramen of Magendie is intermittent, in others it rapidly

becomes complete; in these cases ventricular absorption of the fluid would render the obstruction less complete. That such absorption occurs was clearly demonstrated by Nañagas in his experiments on hydrocephalic kittens. This represents a fourth route by which cerebro-spinal fluid may be absorbed, but under normal conditions this method of escape accounts only for a small part of the fluid.

The Pacchionian Bodies and Arachnoidal Villi

A typical Pacchionian body, such as that shown in fig. 15, which was taken with the surrounding dura mater from a *lacuna lateralis* near the superior longitudinal sinus, consists of a mulberry-like mass of lobules which projects into a depression in the overlying bone. In the specimen figured, the summit of the body appeared to project through an opening in the superficial o

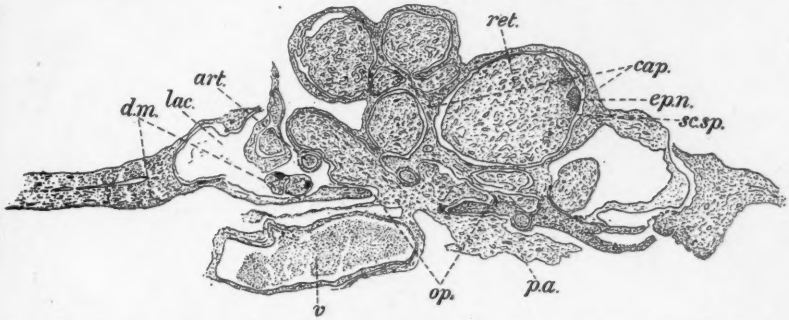

Fig. 15. Vertical section of a Pacchionian body which projected into a lacuna lateralis near the sagittal sinus. *art.*, Arteriole. *cap.*, Capsule of a lobule. *d.m.*, Dura mater. *ep.n.*, Epithelial nodule. *op.*, Opening through the dura mater. *p.a.*, Pia arachnoid. *lac.*, Lacuna. *ret.*, Reticulum. *sc.sp.*, Sub-capsular space. *v.*, Vein in sub-arachnoid space.

endosteal layer of the dura mater, and come into direct contact with the diploic tissue of the bone, the vitreous table having been absorbed. The ragged edges of this opening in the dura mater are represented in the drawing. No membrane could be detected lining the bony pit which lodged the Pacchionian body. The body is composed of a number of lobules each of which is surrounded by a capsule of loose fibrous tissue, continuous with a general investing capsule, and forming interlobular septa where the lobules are in contact. The latter contain small arteries and veins continuous with those in the pia arachnoid tissue which lies between the dura mater and the brain. Branches from these vessels enter the reticular tissue of the lobules, but do not appear to open into either the sub-capsular space or the tissue spaces of the lobules, as no openings into these spaces can be detected, and the spaces contain no blood corpuscles. The interior of each lobule is filled by an oedematous-looking reticular tissue enclosing within its meshes a continuous system of intercommunicating spaces (fig. 16). The reticulum consists of a

loose white fibrous connective tissue, containing fine elastic fibres. The white fibres are feebly stained, wavy, and coiled in all directions. Among the fibres are sparsely scattered, small oval nuclei, which are mesothelial in type. Some of these nuclei are imbedded in the reticulum, others appear to lie on the surface of the fibrillae, and form the nuclei of flattened cells lining the tissue spaces. In some places they are clumped together, forming multinuclear plasmodial

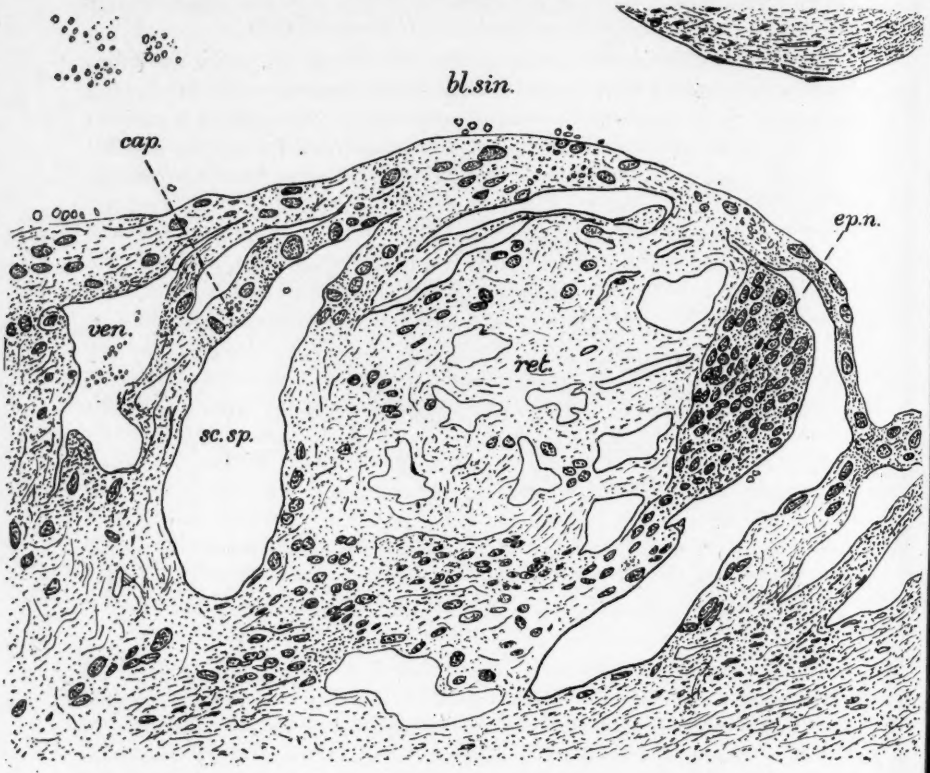

Fig. 16. Section through a lobule of the Pacchionian body shown in fig. 15, highly magnified. *bl.sin.*, Lacuna lateralis. *cap.*, Capsule. *ep.n.*, Epithelial node. *ret.*, Reticulum. *sc.sp.*, Sub-capsular space. *ven.*, Venule.

masses, identical in structure with the nuclear masses which form the mesothelial caps covering the arachnoidal villi (fig. 17). The spaces of the reticulum are lined here and there by flattened mesothelial cells, but these do not appear to form a complete and continuous endothelial covering on the surface of the reticular mass which fills each capsule, nor a continuous endothelium lining the spaces. The inner surface of each capsule, however, is lined by a continuous mesothelium, which forms the outer wall of a sub-capsular space or sinus.

This layer in certain situations is blended with the discontinuous mesothelial layer covering the surface of the enclosed core of reticular tissue, and the multinuclear plasmodial masses. The outer surface of the investing capsule is covered by an endothelial layer continuous at the base of the Pacchionian body with the endothelium lining the lacuna. The sub-capsular and reticular spaces are continuous through the pedicles of the Pacchionian body with the sub-arachnoid spaces on the surface of the brain, but do not appear to be

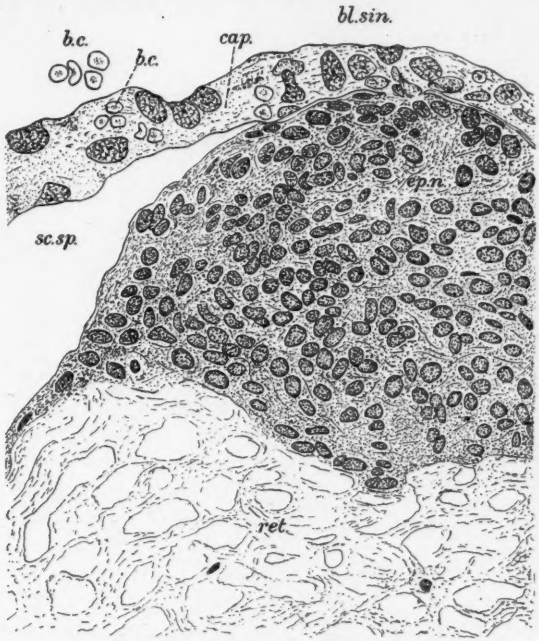

Fig. 17. Epithelial node of a Pacchionian body situated on one of the lobules of reticular tissue and incompletely covered by the capsule which surrounds the lobule. Over the node the capsule has almost disappeared and is represented merely by an endothelial layer which contains a capillary vessel in the lumen of which blood corpuscles are visible. *b.c.*, Blood corpuscles. *bl.sin.*, Lacuna lateralis. *cap.*, Capillary. *ep.n.* Epithelial node. *sc.sp.*, Sub-capsular space.

directly continuous with the lumen of the lacuna. A large vein, shown in transverse section in the drawing, lay in close relation to the Pacchionian body and in the sub-arachnoid tissue, beneath the dura mater.

In some places the multinuclear plasmodial masses on the reticular tissue of the lobules are in direct relation with an endothelial lined space, or a capillary vessel in the overlying capsule, which in these situations is reduced to a thin endothelial membrane (see fig. 17). The capillary vessels contain red blood corpuscles, and open into the general lumen of the lacuna. There is

thus a very intimate connection of the multinuclear masses with the venous system, through which cerebro-spinal fluid might pass into the blood stream. This intimate relation of the "epithelial knots" to the venous sinuses and the passage of a capillary vessel from the epithelial mass have been observed by Le Gros Clark, who has pointed out that even those arachnoidal villi which appear to float freely in the sub-arachnoid space, are attached to the dura mater, and he also believes that arachnoid granulations come into direct contact with the blood of the venous spaces from the first, and that they all reach a venous cavity.

Arachnoidal Villi

These structures, of which the Pacchionian bodies represent overgrowths in advancing years, have been amply described by Weed, who showed experimentally that solutions introduced into the sub-arachnoid space passed through them into the venous sinuses. An arachnoidal villus consists of a projection from the dural surface of the arachnoid. The projection may or may not contain a diverticulum of the sub-arachnoid space, in the latter instance consisting merely of a local proliferation and heaping up of the arachnoid mesothelium. Such proliferations are scattered freely over the surface of the cranial arachnoid, and are lodged in small depressions of the dura mater. They are visible both in film preparations of the arachnoid and in sections. Other villi are in definite relationship with the venous sinuses of the dura mater. In these there is usually a stalk into which the sub-arachnoid space extends. The stalk branches, and gives rise to a number of projections which perforate the dural strands and so come into relationship at many points with the endothelium of the sinus or of one of the lacunae laterales, according to position. At the point of contact the mesothelium and vascular endothelium fuse to form a mass of nucleated protoplasm, the cell-tuft of Weed, which morphologically represents four layers: (1) the sub-arachnoid mesothelium, (2) the endothelium covering the arachnoid, (3) the endothelium which lines the dura and (4) the endothelium of the venous cavity. The branches may be more or less myxomatous in structure, or have a reticular core. Confirming Weed's statement, we have been unable to find villi on the spinal arachnoid.

The question arises, if these structures absorb the cerebro-spinal fluid, are they present in the earlier stages of development at a time when the circulation of the fluid is already established? That is, are arachnoidal villi present in the later months of foetal life?

In a specimen obtained from a $7\frac{1}{2}$-months foetus, in which the upper half of the cranium with its contents was decalcified and embedded in celloidin before the block was cut out, the intracranial relations are undisturbed. Serial sections were stained by the usual methods. The choroid plexuses are well developed, and are covered with cells of a secretory type. The pineal gland is advanced in its development. Owing to the density of the pia arachnoid covering, there is little room for the passage of fluid through the

sub-arachnoid meshes beneath the vault of the skull. This condition is probably connected with the rapid growth of the brain as compared with the skull at a time when the convolutions are beginning to appear, so that the nervous tissue is in close apposition with its membranous coverings. On the other hand, the convolutionary growth is not sufficiently advanced for the so-called flumina of the cerebro-spinal fluid to have appreciable magnitude. The sub-dural space can be identified in places as a cleft. The dura mater is a well-developed

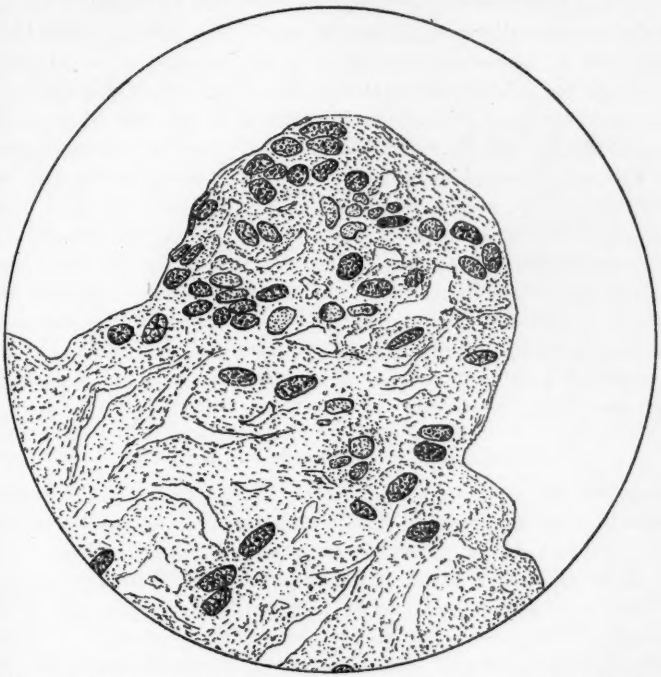

Fig. 18. Arachnoidal villus from the superomesial border of the cerebral hemisphere, near the parieto-occipital fissure. The villus projected into the sub-dural space, and may have been withdrawn from a recess in the dura mater. The tissue spaces of the reticulum are not lined with endothelium, and show no sign of communicating directly with the vascular system. Oval nuclei are grouped in clusters indicating a stage in the development of an epithelial node.

fibrous structure, and lines the bony tissue of the skull. The pia arachnoid beneath it is a single membrane in the region of the convexity of the hemispheres, to which and to the dura it is closely applied. The basal cisternae, as shown by an ordinary dissection of the lower half of the brain, are of moderate size, and during the life of the foetus must have accommodated a fair amount of sub-arachnoid fluid. Whilst in places the arachnoid aspect of the leptomeninx is somewhat folded towards the dura, no definite villi are visible. Neither are there any projections from the arachnoid into the wall of the

superior longitudinal sinus, which already presents its triangular adult shape on cross-section, and, at intervals, receives the openings of lacunae laterales and of cerebral veins. At this stage, therefore, we must assume that the cerebro-spinal fluid is absorbed by some other channel than that of the arachnoidal villi. Moreover, in none of the earlier human and other mammalian embryos in the collection at King's College are arachnoidal villi discoverable.

Flow in the Central Canal of the Spinal Cord

No direct observations on the flow of fluid in the central canal of the spinal cord are possible, hence our knowledge on this point must be deduced from indirect evidence. It is possible that a small amount of fluid may filter through, or be secreted by the epithelium lining the canal, and that since the central canal ends blindly below, and opens into the fourth ventricle above, there may be a slight current which, aided by ciliary movement, will be in an upward direction. It may be noted, however, that the lumen of the cord in old age is frequently obliterated in parts without any subsequent distension of the unobliterated sections of the canal. Hence it is unlikely that the pressure at which fluid is excreted into it, can be that of a true secretion, and it is probable that the main function of the epithelial lining is that of a limiting membrane as elsewhere in the neural canal; and that the force determining the current, if such exists, is produced in the same way as a lymph flow by differences in capillary and venous pressure.

Development of the Foramen of Magendie

Waterston, in 1923 (31), demonstrated the presence of the foramen of Magendie in a human embryo measuring 26 mm. in maximum length, and definitely stated that the opening was not present in an embryo of 17 mm. length. In an embryo of 20 mm. the roof of the fourth ventricle at the future site of the foramen was commencing to break down. He associated the date of its formation with the development and functional activity of the choroid plexuses. Weed (33) had previously associated the appearance of the foramen with the "individual tufting" of the plexuses. Wilson has also described the development of the foramen which appears as a bubble-like protrusion of the thin ependymal roof of the fourth ventricle. This is "blown out," and afterwards ruptures. Further, the opening has been shown by Blake to be present in a number of mammals other than man. It has been stated that the foramen is absent in the horse. We have, however, seen it in the brain of this animal, in which it presented all the features of a natural opening.

In a 20 mm. human embryo (about the seventh week) we have ourselves seen that the perforation constituting the foramen of Magendie is practically established, there being at this stage only the thinnest film of tissue filling the site of the future orifice (fig. 19). In another specimen 22 mm. long the perforation is not yet established, although the dorsal herniation is well developed. At the summit of this protrusion, where the foramen is about to

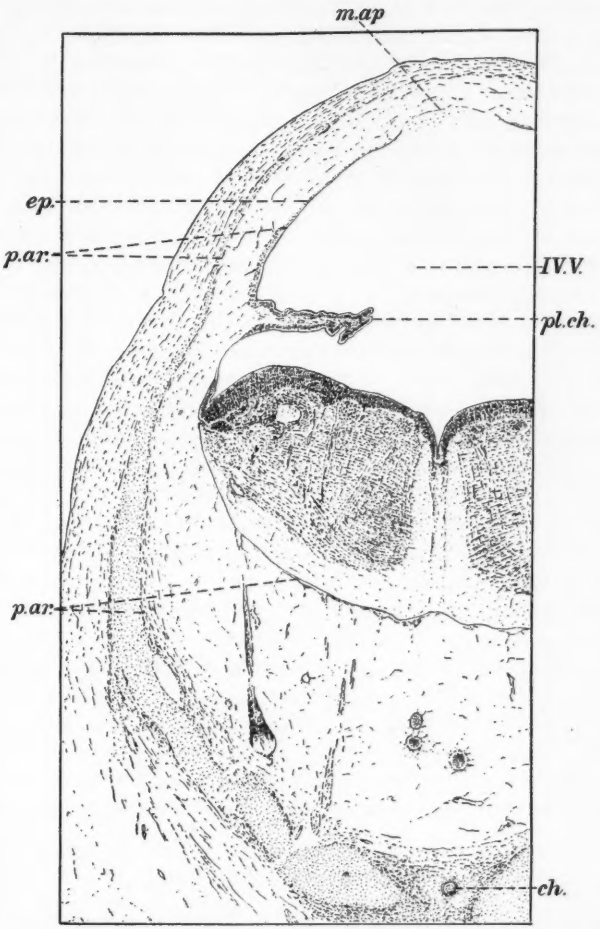

Fig. 19. Coronal section through the fourth ventricle of a 7½-weeks human embryo measuring 20 mm. in length. Degeneration of the epithelium forming the roof of the fourth ventricle at the site of the future foramen of Magendie has already commenced (*m. ap*). The neural tube is surrounded by a loose mesenchymatous tissue. This will afterwards become differentiated into arachnoid membrane, sub-arachnoid tissue, and pia mater. The spaces of the mesenchyme are filled with a tissue fluid, which when the medial and lateral openings of the fourth ventricle are established will be replaced by cerebro-spinal fluid. *IV. V.*, Fourth ventricle. *ch.*, Notochord. *ep.*, Ependyma. *p.ar.*, Pia arachnoid. *pl.ch.*, Plica choroidea.

be formed, there is marked proliferation of nuclei in the ependyma; the cells here are more spherical than elsewhere and are crowded together, whereas in the bulging roof of the ventricle they have been flattened out. The ground substance of the reticulum immediately outside is thickened, so as to form a relatively dense layer superficial to the proliferating ependyma. This condensation of the ground substance is more deeply stained with eosin than the rest of the sub-arachnoid reticulum. These phenomena apparently indicate a reaction to some local irritant, probably the intraventricular fluid, which is soaking through the attenuated ventricular roof. At this early stage of development the fluid in the ventricles presents obvious differences from the adult choroidal secretion; it is highly albuminous, as is shown by the rich coagulum deposited in sections. The very earliest ventricular fluid is included amniotic liquid, which is probably added to by the ependymal layer of the neural tube, or by transudation from the rich sub-ependymal capillary plexus. In the 20 mm. specimen there are well-defined evaginations marking the position of the choroid plexuses in all the ventricles (fig. 19). Moreover, the epithelial cells covering the plexuses contain clear vacuoles and granular material in the cytoplasm, indicating secretory activity. As might have been expected, the differentiation of the plexuses of the fourth ventricle is somewhat in advance of that of the more anteriorly situated cavities of the brain; the cells in the latter situations show fewer secretory appearances, and are arranged in more than one layer. In some human embryos, however, the plexuses of the lateral ventricles are in advance of those of the fourth, in respect of their tufting.

It seems to us that accumulation of intraventricular fluid and consequent mechanical rupture of the roof of the fourth ventricle is not enough to account for the development of the foramen of Magendie; more delicately co-ordinated factors have to be considered. The foramen is prepared for the escape of the choroidal secretion rather than directly caused by it. We have no reason to believe that the secretion has at any time a pronounced digestive action.

Development of the Membranes

In the human embryo of 20 mm. length, referred to above, the distinction between pia mater, arachnoid tissue and dura mater is just commencing. The brain is invested by a loose mesenchyme, which occupies the space between it and its membranous capsule. At this stage the latter forms the vault of the developing skull. Later it gives rise to the dura mater, bony wall of the skull and pericranium. The loose mesenchymatous tissue is especially abundant in the situations of the cisternae of adult life, and at the base of the brain where it is traversed by the cranial nerves and blood vessels. Where the nerves pierce the skull a certain amount of the tissue is carried downwards through the foramina to form their perineural sheaths; but the tissue here is not as loose as elsewhere, and the passage of fluid through its spaces would be less

free than in the sub-arachnoid spaces generally. The mesenchyme consists of a delicate syncytial network containing in its meshes a large amount of tissue fluid. The spaces of this network are the forerunners of the sub-arachnoid spaces, but the cerebro-spinal fluid has not yet established a communication with them. The fluid of the spaces is an embryonic tissue fluid, probably similar to that found at this stage of development in the loose extrapleural and extraperitoneal tissue. A condensation of the mesenchymal tissue, representing the future pia mater, has already taken place on the surface of the neural tube. A similar condensation takes place beneath the membranous capsule, and will form the inner stratum of dura mater, lined by endothelium.

In a human embryo 6 cm. in length, at the third month of intra-uterine life, a considerable advance has taken place in the development of the membranes of the brain and spinal cord. A definite pia mater is recognisable, which consists of a layer of mesothelium which rests directly on the outer limiting membrane of the neural tube. Its superficial surface is directly continuous with the trabeculae of the pia arachnoid tissue which contains numerous thin-walled arterioles and venules. The walls of these vessels consist of an endothelial lining, covered by loose adventitia which is continuous with the supporting strands of the trabecular tissue. Both arterioles and venules are flattened, but are not completely collapsed. Numerous capillary vessels are present in the trabeculae. The pia arachnoid tissue is limited externally by a continuous layer of mesothelium, the outer epithelial layer of the arachnoid membrane, formerly described as the parietal layer. External to this is a similar mesothelial layer, the endothelium lining the inner surface of the dura mater. Between these two layers is the potential subdural space. No arachnoidal villi are present at this stage of development, nor are arachnoidal cell-nests visible in the fibrous tissue of the dura mater.

Homologies of Brain and Eye

An analogy has been drawn by Wegefarth and others (35) between the cerebro-spinal fluid and the aqueous humour. In chemical composition they are closely similar; the salt, sugar and protein content are approximately the same. It has been stated, however, that the aqueous will contain antibodies, such as agglutinins, when these are present in the blood; haemolysins, nevertheless, do not pass into the aqueous. The cerebro-spinal fluid, on the contrary, is said never to contain antibodies in the true sense of the word, although, as is well known, it frequently gives the complement-fixation test. There is a similar paucity of cells in the two liquids.

Wegefarth and Weed (36) have drawn definite homologies between the fluid systems of the eye and of the cerebro-spinal axis, as shown in the subjoined table:

Eyeball	Brain and its membranes
Sclera	Dura
Pectinate ligament	Arachnoidea
Uveal tissues	Pia mater

Vascular choroidea Descemet's membrane Pectinate ligament	Pia arachnoid of Robertson
Ciliary body	Choroid plexuses
Aqueous humour	Cerebro-spinal fluid
Sinus venosus sclerae	Venous sinuses of dura
Pupil	Rhombencephalic metapores
Posterior chamber	Sub-arachnoid cisterns

The homologies, however, are not complete in every detail and we wish to draw attention to the relation of the secretory epithelium of the ciliary processes to the cleft which in the adult represents the cavity of the primary optic vesicle. This cleft, for the most part only a potential space, lies between the outer pigment layer of the pars ciliaris retinae and the inner layer; which layer is continuous behind, at the ora serrata, with the pars nervosa retinae, and in front and internally with the posterior layer of the pars iridica retinae. If the homology between the secretion of the cerebro-spinal fluid by the choroid plexuses into the ventricles of the brain, and the secretion of the aqueous humour were complete the latter would be secreted into the cleft between the epithelial layers of the ciliary processes. It is, however, secreted into the posterior chamber, which is a mesothelial cavity, and not comparable with the ventricular cavities of the brain. It is very difficult to decide whether both layers, or if only one, which of these two epithelial layers of the ciliary processes is the true secretory agent, but Treacher Collins has shown, by means of bleached specimens, that gland-like tubules dip into the stroma from the outer layer; we have prepared bleached sections of the pig's eye, but in these specimens, although depressions exist between the processes, no definite secretory tubules are present, in the sub-epithelial connective tissue (fig. 21). There is, however, a considerable number of large ovoid cells, which are sometimes isolated, at other times arranged in rows at right angles to the surface epithelium but not directly continuous therewith. While pigmented cells are not, as a rule, associated with secretion, yet in the case of the ciliary body they are the cells next the blood vessels and must be taken into account as the fluid and other constituents of the aqueous humour derived from the plasma circulating in the blood vessels would have to pass through them and would probably be modified thereby. The same applies to the inner unpigmented layer of cells; in them, moreover, the nuclei are placed next the cleft, i.e. towards the pigmented lamina, while the clear and presumably secretory cytoplasm lies mainly next the posterior chamber; it is only in the most intense forms of secretion that the nucleus of the cell comes to lie next the lumen of a glandular acinus (fig. 20). It is thus apparent that a diffuse process of filtration or of secretion through the wall of the neural tube has here replaced the passage through definite foramina as in the case of the fourth ventricle.

The pupil does not correspond to the foramina of exit from the ventricles (rhombencephalic metapores), as it represents the opening of the secondary optic vesicle; moreover it is not formed by a rupture or absorption of the neural epithelium or ependymal wall, but lies between two mesothelial spaces, both of which correspond to the sub-arachnoid space.

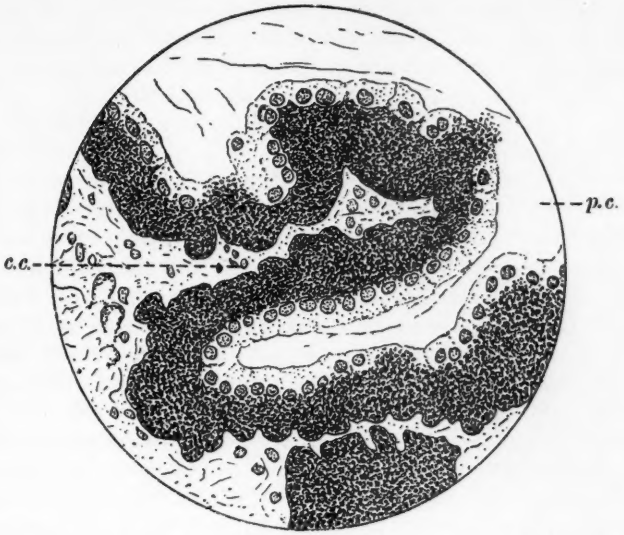

Fig. 20. Section through the ciliary processes showing the superficial stratum of clear cubical cells and a deeper layer of epithelial cells, the nuclei and outlines of which are completely obscured by pigment granules. The separating line between the epithelial layers, which represents the cavity of the primary optic vesicle, is similarly obscured. *c.c.*, Central core of vascular connective tissue. *p.c.*, Posterior chamber.

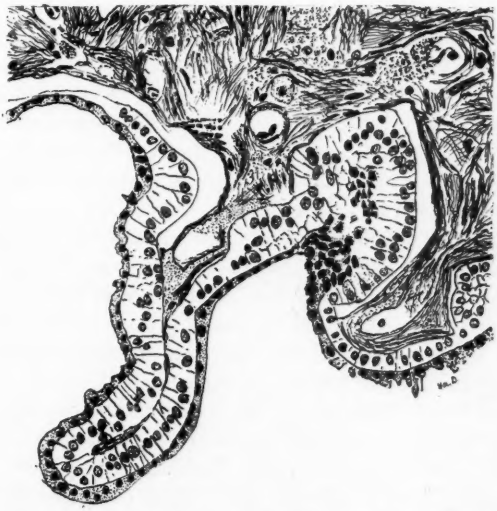

Fig. 21. Section through the bleached ciliary processes of a pig's eye showing one of the gland-like depressions of the epithelial covering.

Of interest in connection with the homologies of the brain and eye, is the occasional occurrence of pigmentation of the arachnoid membrane, especially the spinal arachnoid, quite apart from disease (Risien Russell(27)). It is possible that the choroid is the phylogenetic ancestor of the arachnoid; for the eye looms large in the evolution of the nervous system, and the choroid appears in the zoological scale before the arachnoid.

Significance of the Cerebro-spinal Fluid

In addition to performing mechanical functions, the cerebro-spinal fluid receives waste products from the nervous system, so that the fluid absorbed from the sub-arachnoid space may be regarded as diluted lymph. The peculiarities in origin and composition of the fluid are hardly surprising when the metabolic characteristics of nervous tissue are borne in mind. The energy changes are minute, the most obvious being the electrical variations which occur with excitation. In peripheral nerves Tashiro found only small respiratory changes, yet in the case of the central nervous system (especially) they are essential for the continued existence of nervous integrity. Interference with these changes, even for a short space of time measurable in minutes, will, as the experiments on cerebral anaemia and asphyxia show, cause disintegration and death. In this connection the elementary fact that the blood in the sagittal sinus is venous in colour seems often to have been forgotten.

Notwithstanding the very delicate thermopyles which have been employed, it is only recently that Downing, Gerard and A. V. Hill[1] have detected heat production in nervous tissue as a result of excitation. The formation of nitrogenous and phosphatic waste products by the neural substance, though it must be assumed to occur, has at the present time not been demonstrated, in spite of innumerable observations on the urine in conditions of cerebral activity. The nervous system is generally regarded as an organ concerned with the co-ordinate liberation and inhibition of energy from the effector systems, rather than a source of the manifest energy of the body. The immaterial activities of the mind can require but little physical energy, measured as heat, for their functioning, and a large part of the cortex cerebri is occupied with mental processes. Hence we find that such waste products as result from neural metabolism are but scanty, though more or less constant in amount, and that the watery fluid escaping from the ventricles into the sub-arachnoid spaces is not greatly enriched by the additions it receives from the perivascular liquid. That the choroidal secretion itself is so watery is not very unusual or surprising, since apart from mucus, animal secretions are not generally rich in proteins.

The ventricles may have developed to their relatively spacious capacity in order to contain the choroid plexuses and their secretion, forming a sort of reservoir for the latter. Regarding the ventricles as the duct of the choroidal plexuses the analogy to a gland is practically complete; for although infoldings into the duct have replaced the more usual out-buddings in the pro-

[1] *Proc. Roy. Soc.* B., 100, p. 223, 1926.

cesses of development, this is not a unique example of such and a very similar condition is found in the developing renal glomeruli. A mechanical reason for the infolding of the plexuses into the ventricles, rather than outward into the nerve-substance, is possible, for the resistance in the ventricles is comparatively slight; but that much more complicated factors are concerned cannot be doubted.

The cerebro-spinal fluid formed by the choroid gland has been variously regarded as a true secretion, or as a product of dialysis (Mestrezat (21)), or of filtration. The paucity of solid constituents in the fluid cannot be used as an argument in favour of the purely physical hypothesis of its origin, for parotid saliva contains 0·5 per cent. or less of solids, and is undoubtedly a true secretion, although here we have the formation of a specific ferment, ptyalin. Nevertheless, the secretory pressure of saliva is considerably higher than the pressure of the blood in the arteries supplying the salivary gland, whereas the reverse is true of the cerebro-spinal fluid (see table). The crucial test of secretory activity as opposed to a mechanical process, viz. the utilisation of oxygen during the secretory act, is not easily applicable to the choroid plexus. The fact that increased formation of cerebro-spinal fluid takes place when choroid plexus extract is injected into the blood stream (Dixon and Halliburton) is a point in favour of secretion, although it might possibly be explained as resulting from dilatation of choroidal blood vessels. Mott (22) described nerve fibres on the arteries of the plexuses.

The cerebro-spinal fluid has often been likened to the lymph. More likely, however, the true lymph of the brain is the perivascular fluid, which is added to the cerebro-spinal fluid in the sub-arachnoid space. Moreover, whereas the lymph of the body generally is poured into the venous system through a few definite openings, the sub-arachnoid fluid, containing the cerebro-spinal lymph, enters the blood stream by a multiplicity of channels, each of which is closed by an endothelial membrane. These, the arachnoidal villi, are formed as secondary connections, sprouting from the arachnoid membrane towards the lumen of the sinuses. This has some bearing on the development of the main lymphatic system, concerning which there has been so much dispute.

There is a considerable difference in the distribution of the carbon dioxide of cerebro-spinal fluid as compared with that of lymph. Thus Mott (22) found that the total percentage of this gas, i.e. the amount obtainable by the addition of dilute acid and ebullition *in vacuo*, was the same in the two fluids, viz. 50 per cent. by volume. However, of the total percentage in cerebro-spinal fluid only 10 per cent. was unfixed and so obtainable by simple ebullition *in vacuo*, the remaining 40 per cent. being fixed and so unobtainable without the addition of acid. Lymph, on the contrary, normally contains only 4 per cent. of fixed CO_2, but 46 per cent. of free CO_2. These differences are not easily understood, but to us they suggest a secretory rather than a purely physical selective activity on the part of the cells of the choroidal epithelium, either with reference to the gas itself or relating to some chemical substance capable of fixing the gas in the cerebro-spinal fluid.

Ventricular Puncture

Any consideration of hydrocephalus leads to a criticism of ventricular puncture. This operation, while of undoubted value as a diagnostic procedure in certain cases, has been performed rather indiscriminately. Septic meningitis is set up in some cases when the puncture is made without previously trephining the skull; in this method a small hole is bored through scalp, skull and dura by means of a drill, grooved to receive the stylet subsequently inserted. There is a tendency to carry out these manipulations in a general ward and with only a small area of the head shaved and purified. Organisms introduced into the ventricles are carried to all parts of the sub-arachnoid cavity by the normal current of the cerebro-spinal fluid, and therefore meningitis may be disseminated with dramatic swiftness. Moreover, when ventricular puncture is carried out by this, which may be called the subcutaneous method, there is a real danger of wounding the veins on the surface of the hemisphere. In one case which has come under our notice this accident occurred, and death ensued a few hours later from cerebral compression; post-mortem there was found a clot the size of a saucer deeply indenting the brain. These dangers are obviated if trephining is done first and a view of the cerebral vessels obtained thereby.

When a puncture is done in order to determine whether a ventricle is dilated or not, there is an evident chance of missing a normal ventricle and so injuring the corpus striatum.

To determine the situation of the block in cases of hydrocephalus, phenol-sulphonephthalein has been injected into the ventricle and the absorption into the blood and passage into the sub-arachnoid space studied. In view of the scientific operations of Dott and Frazer, such diagnostic measures seem highly justified. With regard to ventricle-puncture as a means of obtaining pneumo-radiograms of the ventricles as a routine method, though in certain cases it is of undoubted value, less can be said in support.

As a therapeutic operation tapping of the ventricles has well-known risks. In infants, fatal haemorrhage into a dilated ventricle is by no means a rare result of the operation, especially if all the cerebro-spinal fluid has been withdrawn.

SUMMARY

1. The specimen which we have described represents the type of hydrocephalus commonly known as "congenital."

2. It shows signs of inflammation of the choroid plexuses, membranes of the brain, and brain substance.

3. The irritative or inflammatory process appears to be of long standing and to have commenced as a pre-natal condition, as is evidenced by proliferative and degenerative changes in the vessel walls, nerve tissues and membranes,

the presence of corpora amylacea and corpora arenacea, and interference with the normal development of the brain.

4. The choroidal veins were distended with blood clot.

5. The chronic inflammatory process was, in our opinion, the primary cause of the hydrocephalus, and this, with the accompanying deformations, was not due to a germinal defect.

6. Such terms as "idiopathic," "essential," and "congenital," when applied to this type of hydrocephalus, are misleading, although the term "congenital," if not used in contradistinction to "acquired," is not incorrect.

7. The occurrence of hydrocephalus in several members of the same family is not evidence of the disease being transmitted hereditarily from parent to offspring, but may be explained on the assumption that the same toxic condition or disease, e.g. maternal syphilis, has acted in the same manner in succeeding pregnancies.

8. The median and lateral apertures of the fourth ventricles are natural openings and not artefacts. We have been unable to confirm the presence of a natural opening in the descending horn of the lateral ventricle.

9. Secretion of the cerebro-spinal fluid normally takes place directly into the sub-arachnoid space by means of the cornucopia, as well as into the ventricles.

10. Some part of the wall of the neural tube may rupture, e.g. the roof of one or both of the cerebral hemispheres, or the roof of the mid-brain, yet the ventricles may continue to enlarge. Further, the enlargement may take place subsequent to the drainage of a spinal meningocele.

11. Distension of the ventricles of the brain may arise in the absence of any obstruction of the aqueduct of Sylvius or closure of the foramina in the roof of the fourth ventricle.

12. The ependyma lining the ventricles may be destroyed by disease or in old age so that a free communication occurs by way of the spaces in the sub-ependymal reticular tissue between the intraventricular fluid and the intracerebral fluid contained in the perineuronal and perivascular spaces.

13. A communication by means of the perivascular spaces normally exists between the perineuronal spaces and the sub-arachnoid cavity.

14. Although the greater number of the vessels in the pia mater covering the brain and spinal cord consists of thin-walled arterioles and venules, the connecting capillaries of which are situated in the underlying nervous tissue, capillaries are undoubtedly present in the pia arachnoid. They are surrounded by a thin sheath of connective tissue.

15. Arachnoidal villi are present on the surface of the human arachnoid next the dura mater of the cranium. They do not appear to be present, however, on the spinal arachnoid.

16. Large tissue spaces are present in the embryonic pia arachnoid prior to the development of the foramina in the roof of the fourth ventricle.

17. Absorption of cerebro-spinal fluid appears to take place by three routes:

(*a*) Through the arachnoidal villi into the venous sinuses.

(*b*) Into the capillaries and venules of the leptomeninges.

(*c*) By the perineural lymphatic vessels.

18. The flow in the perivascular spaces is probably under normal conditions outward in direction, though it is capable of reversal.

One of us is at present engaged in the study of a specimen of occipital meningocele which is of some interest as throwing light on the continued production of cerebro-spinal fluid apart from its formation as a secretion of the choroidal epithelium. It is to be hoped that the complex problems of the relations of secretion to absorption of the cerebro-spinal fluid will, as a reward of the labours of the many workers engaged in its study, at some not far distant date be more completely solved than they appear to be at present.

A practical outcome of our own work appears to be the importance of careful ante-natal hygiene in the prevention of "Congenital Hydrocephalus."

REFERENCES

(1) Blackfan, K. D. *Vide* Dandy, W. E.

(2) Bland-Sutton, J. (1924). *Orations and Addresses.* London, W. Heineman, pp. 108 *et seq.*

(3) Cleland, J. (1896). *Human Anatomy, General and Descriptive.* By Cleland and Mackay p. 608.

(4) Cushing, H. (1914). "Studies in the Cerebrospinal Fluid." *Journ. Med. Research,* vol. xxxi, pp. 1 *et seq.*

(5) —— (1925). "Cameron Lectures. I. The Third Circulation and its channels." *Lancet* vol. ii, p. 851.

(6) Dandy, W. E. (1918). *Annals of Surgery,* p. 569.

(7) Dandy, W. E. and Blackfan, K. D. (1913). "An experimental and clinical study of Internal Hydrocephalus." *Journ. Amer. Med. Assoc.* vol. lxi, p. 2216.

(8) Dixon, W. E. and Halliburton, W. D. (1910). *Journ. Physiol.* vol. xl, p. xxx (*Proc. Phys. Soc.*); *Journ. of Physiol.* 1913, vol. xlvii, No. 3, p. 215.

(9) Dott, N. and Frazer, J. (1922–3). "Hydrocephalus." *Brit. Journ. Surgery,* vol. x, p. 165.

(10) Gask and Wilson (1920). *Surgery,* p. 368.

(11) Greenfield and Carmichael (1925). *The Cerebrospinal Fluid in Clinical Diagnosis.*

(12) Halliburton, W. D. (1889). "Cerebrospinal Fluid." *Journ. Physiol.* vol. x, p. 232.

(13) Hill, Leonard (1909). "The Vascular System and Blood Pressure." *Further Advances in Physiology.* Arnold. p. 137.

(14) —— (1896). *Physiology and Pathology of the Cerebral Circulation.*

(15) Hilton, J. (1880). *Rest and Pain,* p. 18.

(16) Huber, G. Carl. "Observations on the Innervation of the Intracranial Vessels." *Journ. Comp. Neur.* vol. ix.

(17) Key and Retzius (1876). *Anatomie des Nervensystems und des Bindesgewebe.* Stockholm.

(18) Le Gros Clark, W. E. (1920). "On the Pacchionian Bodies." *Journ. Anat.* vol. lv, p. 40.

(19) Macleod (1920). *Physiology and Biochemistry in Modern Medicine,* 3rd ed. p. 255.

(20) Margulis (1912). *Arch. für Psychiat.* vol. i, p. 31.

(21) Mestrezat, W. (1912). *Le Liquide Céphalorachidien.* Paris.

(22) Mott, F. W. (1910). "The Cerebrospinal Fluid." *Lancet,* vol. ii, p. 1.

(23) NAÑAGAS, J. C. (1921). "Experimental Studies on Hydrocephalus." *Johns Hopkins Hosp. Bull.* vol. XXXII, p. 381.
(24) PACCHIONIUS, ANTONIUS (1721). *Dissertationes Physico-anatomicae de Dura Meninge Humana.*
(25) POIRIER and CHARPY (1907). *Traité d'Anatomie Humaine.*
(26) RETZIUS, G. *Vide* Key, A.
(27) RISIEN-RUSSELL, J. S. (1910). "Diseases of the Spinal Meninges." Albutt and Rolleston's *System of Med.* vol. VII, p. 618.
(28) SARGENT, P. (1911). "Some Points in the Anatomy of the Intra-cranial Blood Sinuses." *Journ. Anat. and Phys.* vol. XLV, p. 69.
(29) STÜRMER, R. (1913). "Die 'Corpora Amylacea' des Zentralnervensystems." *Histologische und Histopathologische Arbeiten*, Bd. v, Heft 3, S. 417.
(30) SWANZY, H. R. (1892). *Handbook of Diseases of the Eye*, pp. 408, 412. Also recent editions edited by Werner, L.
(31) WATERSTON, J. (1923). *Proc. Anat. Soc. Great Britain and Ireland*, vol. LIX, p. 67.
(32) WEBER, L. W. (1906). *Arch. für Psychiat.* vol. XLI, p. 64.
(33) WEED, L. H. (1914–15). *Journ. Med. Research*, vol XXXI, pp. 21–175.
—— *Contributions to Embryol. No.* 14, *Carnegie Inst.* No. 225.
—— (1920). *Johns Hopkins Hosp. Bull.* vol. XXI, p. 343.
—— (1920). *Carnegie Inst. Washington*, No. 272, p. 425.
(34) WEED, L. H. and MCKIBBEN, P. S. (1919). *Amer. Journ. Physiol.* vol. XLVIII, p. 512.
(35) WEGEFARTH (1914–15). *Journ. Med. Research*, vol. XXXI.
(36) WEGEFARTH and WEED. *Ibid.*
(37) WISLOCKI and PUTNAM (1921). *Amer. Journ. Anat.*

THE COMPARATIVE ANATOMY OF THE LATERAL GENICULATE BODY

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THE present enquiry grew out of an investigation carried out by one of us on the form of the lateral geniculate body and retina in some of the Primates (5). In attempting to correlate the form of the lateral geniculate body with the type of retina (rod-cone or rods only) and the presence of a macula and fovea it was observed that the form of the lateral geniculate in a lemur such as *Nycticebus* appeared to be quite different from that of *Tarsius* or the marmoset or from that of an Insectivore like *Tupaia* (a form closely allied to the Primates (3)). It occurred to us that the differences observed might be due to the nocturnal habits of this animal. In order to investigate this further it was decided to study the form of the lateral geniculate in a number of Primates. The post occupied by one of us[1] gave us access to the material at the Zoological Gardens and enabled us to carry out the investigation.

The general assumption (2) from which we started was that the lateral geniculate body consists of two portions, viz. a ventral nucleus composed of small nerve cells diffusely scattered, not arranged in any laminated pattern and probably concerned mainly with the mediation of mid-brain reflexes; and secondly a dorsal nucleus composed of larger cells arranged in a definite laminated pattern connected with the visual cortex, the elaboration of this nucleus being related to the differentiation of the retina. On this basis we were able to establish a series in the animals studied and suggest that the final elaboration takes place in the dorsal nucleus when the macula and fovea appear in the retina. Other parts are described in relation to the lateral geniculate body such as the nucleus pregeniculatum, the nucleus perigeniculatum and the nucleus transversus peduncularis. These are small and their particular significance, if any, is unknown. In the previous investigation already referred to (5), it appeared that the lateral geniculate body in *Nycticebus* assumed a form that did not fit into this scheme. For in the assessment of the areas of the lateral geniculate of this creature, it seemed that the so-called ventral nucleus was much larger than the dorsal and moreover was composed of large cells that assumed a definite laminated arrangement. The dorsal

[1] J. Beattie.

nucleus was of similar composition but unlike all the other specimens was much smaller than the ventral part.

It therefore seemed as if the general plan of the composition of the lateral geniculate was invalid or that a different form was assumed in creatures of different habit. The point was of some importance and further investigations were desirable.

The material which we studied consisted of the lateral geniculate body of the following Primates: (1) *Lemur fulvus*, (2) *Lemur niger*, (3) *Galago*, (4) *Perodicticus potto*, (5) *Nyctipithecus felinus*.

The lateral geniculate bodies with the adjacent parts of the brain stem were cut transversely and sections 15μ thick were stained in toluidin blue. All the brains had been fixed in 10 per cent. formalin.

DESCRIPTION OF THE FORM OF THE LATERAL GENICULATE BODY IN THE DIFFERENT SPECIMENS

(1) *Lemur fulvus*. The cranial extremity of the lateral geniculate shows an apical and two medial prolongations, these latter being directed towards the ventral nucleus of the thalamus. A series of large cells form a circular ring around the periphery of the lateral geniculate except ventro-medially where they are more diffuse and smaller. Inside this peripheral lamina there lies a smaller internal lamina. When traced caudally the mass of the body grows larger and the cells, which more cranially were scattered, now lie closer together and form a series of laminae in a dorso-ventral direction. Four laminae are thus formed. The medial prolongations appear larger.

At the middle of the body the form assumed resembles that of *Nycticebus*. There is a dorsal prolongation and a ventral portion with a medial prominence. The cells are all large except in the ventro-medial corner where they are smaller and somewhat scattered.

In the caudal sections the volume of the body grows smaller. The dorsal prolongation is much reduced and the outline of the body as a whole is nearly circular. It is difficult to separate the lateral geniculate from the thalamus. The cells are large and no differentiation into dorsal and ventral nuclei from the size and arrangement of the cells is possible.

This specimen resembles pretty closely the arrangement described in *Nycticebus*. The retina has been studied and the results published elsewhere (6). It is a rod retina heavily pigmented.

(2) *Lemur niger*. The lateral geniculate begins as a circular mass of closely packed cells. These are large and show no definite arrangement. Further caudally the volume increases and the form changes. The fibres of the optic tract spread widely and reach all parts of the lateral geniculate. Between the medial and lateral parts of the optic tract there are small scattered cells which bend round the pes pedunculi and become continuous with the substantia nigra. The cells composing the mass of the lateral geniculate form a peripheral

and central series. They are of uniform size and there is no division of the nucleus into dorsal and ventral portions.

Further caudally there appear a dorsal prolongation, a medial projection and a ventral mass of cells. The medial and lateral walls are laminated. In the ventro-medial corner a separate mass of cells accumulates. Between the two there is a wide area in which the cells are less abundant.

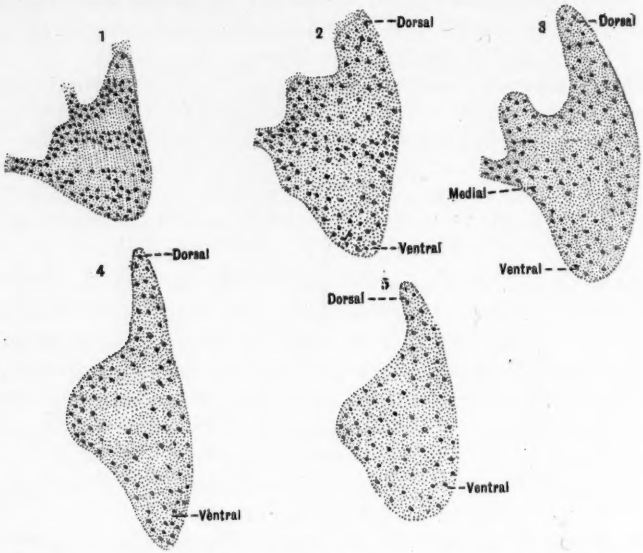

Fig. 1. Schematic representation of the form of the lateral geniculate body of *Lemur fulvus*. Numbers 1–5 represent outlines of the body in a cranio-caudal direction.

At its middle the lateral geniculate appears transversely expanded. The optic tract expands widely, forming a cup in which the lateral geniculate sits. The lateral geniculate consists of a series of laminated cells in which those nearest the optic tract are better defined than those more remote. In all there are four laminae. The two ventral laminae are clear cut. In these there are interspersed large cells—most abundant in the medial portions. Indeed in the medial part they are to be found in all laminae. The laminae furthest from the optic tract look more confused because the cells are more numerous and the margins less defined. There is nothing that can be called a ventral and a dorsal nucleus. The form of the body remains constant and the cell characters described retain the same distribution.

If we regard the transverse expansion of the body as being homologous with the dorso-ventral disposition of the lateral geniculate then the medial part in this animal corresponds with the ventral in others and the lateral part with the dorsal. The ventral and lateral parts would then contain the large

cells and the medial part would not be so well laminated as the lateral area. The lateral geniculate in this animal is then characterised by the absence of segregation into a ventral and a dorsal nucleus of different form and cell type. The orientation is such that it is transversely expanded. The presence of these conspicuously large cells has also been observed in *Galago*.

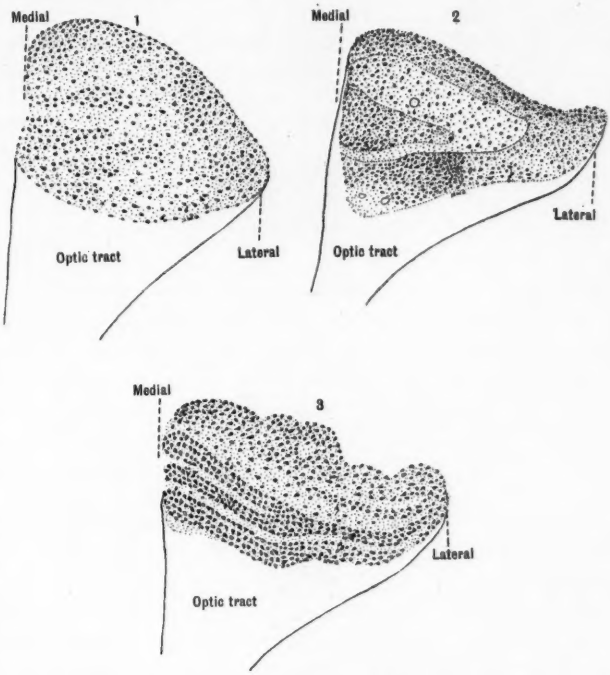

Fig 2. Schematic representation of the shape, laminae, and distribution of large cells in the lateral geniculate body of *Lemur niger*. The numbers indicate cranio-caudal sections.

(3) Bushy-tailed *Galago*. The lateral geniculate is first identified as a transversely expanded group of cells in the course of the optic tract. It soon expands, becoming much thicker medially than laterally. Both portions are composed of medium sized cells. The cells appear to be more characteristically stellate in this animal than in the others studied. A tendency to lamination is apparent at the cranial extremity and above the lateral half there appears a small-celled mass—possibly the corpus pregeniculatum. As the body is followed in section caudally it grows in size and the corpus pregeniculatum soon disappears. It becomes triangular in shape, the base is directed medially and the apex laterally. The lamination is well marked. A peripheral double lamina and a central basal part can be distinguished. The cell character is

uniform. Further caudally the body increases and conspicuously large cells now appear in the ventral median portion. The lamination is very well defined and each row has its own characteristics. The first dorsal row is broad and consists of small cells. The next row is less defined and its cells are scattered. The third row is compact and consists of larger cells. The two ventral laminae fade out in a narrow band laterally while medially they expand and form two rows with quite large cells.

Without further change of character the nucleus grows smaller as it is traced caudally and finally ceases. Nowhere is there developed a dorsal and a ventral nucleus.

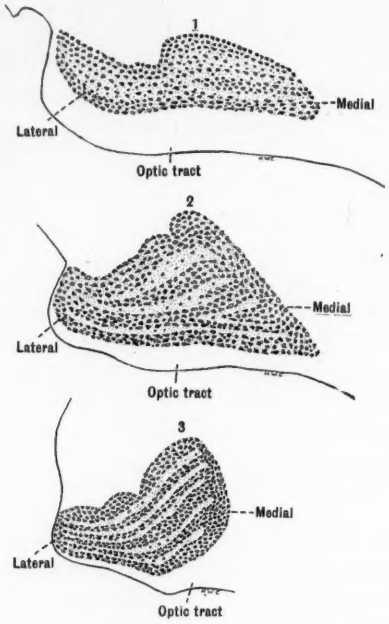

Fig. 3. Schematic representation of the lateral geniculate body of *Galago*. The numbers represent cranio-caudal sections.

(4) *Perodicticus potto.* At the cranial extremity there is a corpus pregeniculatum. When the lateral geniculate begins it is divided into a ventral and a dorsal portion by the presence of a blood vessel. The dorsal half already shows some trace of lamination; the ventral half, broader than the dorsal, has not yet acquired any lamination. Soon the nucleus forms a homogeneous mass, the character of the cells being uniform and the lamination being best marked along the lateral part of the body.

When the middle of the lateral geniculate is reached there appears a very definite small-celled ventral nucleus extending in a caudal and ventral

direction. In contradistinction to the specimens already described *Perodicticus* appears to possess a dorsal nucleus not very well laminated but characterised by large cells, and a small-celled ventral nucleus.

(5) *Nyctipithecus felinus.* Elsewhere one of us (6) has described the structure of the retina and recorded that although this animal is a true South American monkey it possesses a retina composed entirely of rods and without a macula and fovea.

The lateral geniculate appears first as a compact mass of cells in the infero-lateral part of the optic tract. A large part of the fibres of the optic tract pass medially to this group of cells and reach a second group that lies dorsal to the lateral geniculate. When followed caudally the lateral geniculate expands. The dorsal part becomes much reduced. The lateral geniculate is completely embraced by the fibres of the optic tract, and shows a peripheral mass of cells and a basal central mass. The cells are all of medium size and there is no segregation into dorsal and ventral nucleus. The cells are well stained pyramidal or triangular in shape. More caudally the increase in size is manifest. The dorsal portion, horseshoe-shaped, embraces the central basal laminated portion. The lamination of the dorsal portion is not so well marked as in the central mass of cells. When the body is examined a little further caudally the lamination of the dorsal embracing portion has become very sharp and the central part, which is also well laminated, is separated from the dorsal portion by a wide space which is occupied by small scattered cells. This character soon alters as the sections are followed further caudally. The lateral bilaminar portion of the dorsal part is still evident but medially this part has been replaced by a great expansion of the central basal mass. Dorso-medial to the body there appears for the first time a group of small irregularly arranged cells. The central basal part has become much expanded and its character marks it off sharply from the remaining portion of the dorsal. Its cells are individually larger and are more loosely arranged, compared with the lateral dorsal part where the cells are smaller and more closely packed together. This condition is preserved until one approaches the caudal extremity of the body. The lateral bilaminar portion undergoes rapid reduction. The central part has become much reduced. Its lateral portion has become thin and runs parallel with the remains of the lateral portion of the dorsal part. The most medial part of the central portion has become reduced to a few scattered large cells, and replaced by a collection of irregularly arranged small cells representing the ventral nucleus. The dorso-medial part mentioned above as a group of scattered cells has become much larger and though still defined by a narrow acellular zone from the lateral geniculate, it has come to occupy some of the area this body previously occupied. As the reduction of the lateral and central portions becomes more and more complete the area is occupied by the expansion of this dorso-medial group. Its small scattered cells come right up against the remnant of the central and lateral dorsal portions of the body. This large dorso-medial mass, which is circumscribed by a narrow

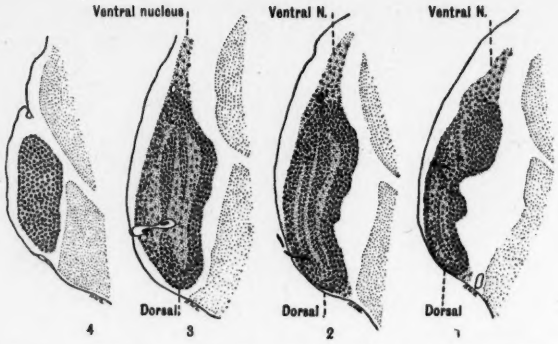

Fig. 4. Schematic representation of the lateral geniculate body of *Perodicticus potto*. Sections numbered cranio-caudally.

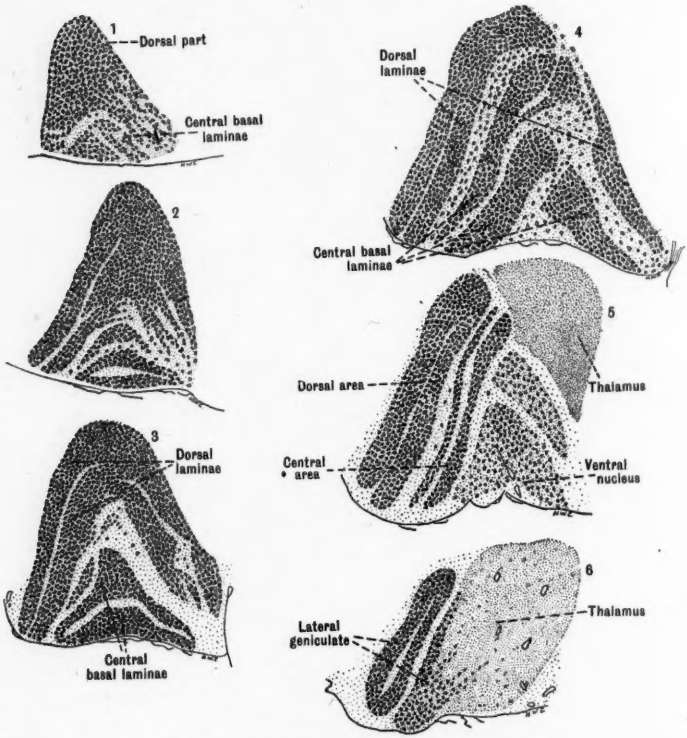

Fig. 5. The lateral geniculate of *Nyctipithecus felinus*. The sections are numbered cranio-caudally.

acellular zone, is composed entirely of small cells which assume no regular arrangement. It extends caudally beyond the remnant of the laminated parts and then it too comes to an end. This cellular mass is really part of the thalamus. It receives optic fibres. This would mean that a large part of the thalamus extends beyond the lateral geniculate body.

In the lateral geniculate of *Nyctipithecus* there is to be discerned a corpus pregeniculatum. This is followed by a nucleus consisting of a dorsal laminated series of cells embracing a central basal laminated area. The central basal area is the more definite portion with the larger cells more widely spaced. First the dorsal portion undergoes reduction and is replaced by an expansion of the larger celled central basal area. Then this becomes reduced and is replaced by small irregularly arranged cells of the ventral nucleus. Finally the lateral geniculate is replaced by a caudal extension of the thalamus.

DISCUSSION

A review of the foregoing results indicates that the lateral geniculate assumes two forms. In one there is a division of the body into two portions of different pattern—a more dorsal laminated portion with medium and large cells and a ventral part in which the cells are smaller and are not arranged in laminae. In the second the lateral geniculate is a homogeneous structure with a tapering dorsal elongation and a thicker ventral part. The cells are for the most part uniform and the whole structure is laminated. To the former type the lateral geniculate of *Perodicticus* and *Nyctipithecus* belong; to the latter the lateral geniculate of *Lemur fulvus*, *Lemur niger*, and *Galago*. It is to be noted that the lateral geniculate is not always directed dorso-ventrally but may lie in a transverse plane. This is notably the case in *Galago*. There is of course no difficulty in making the adjustment so that homologous areas are compared. One other feature is the presence of quite large cells in the ventral and lateral portions of the body, particularly in *Lemur niger* and *Galago*.

If we add to the above specimens those which have previously been described (5), *Tarsius* and *Tupaia* belong to the former class and *Nycticebus* to the second. We had expected to find that these two types of lateral geniculate might correspond with the habits of the animals and be dependent on the structure of the retina. The first type is the phylogenetically old type and has been described in animals other than the Primates (2). The second type is to be regarded as aberrant and specialised. The difference in visual function that might explain the difference in type is the adaptation of the retina for function at different degrees of luminosity. In other papers an analysis (Woollard (5, 6)) of the structure of the retina in a large number of Primates has been made. These results combined with the type of lateral geniculate may be summarised as follows:

Specimen	Retina	Lateral geniculate
Tupaia. (An Insectivore with Primate affinities [Le Gros Clark (3) and others].)	Diurnal retina Rods and cones	Type 1
Tarsius	Rod retina Specialised central area (5)	Type 1
Perodicticus. (One of the Lorisinae and near the Primate stem.)	Not studied	Type 1
Nyctipithecus. (A Platyrrhine monkey, nocturnal, many prosimian features, [Weber (4)].)	Rods only, no cones, no macula or fovea	Type 1
Lemur fulvus	Rods only (6)	Type 2
Lemur niger	Rods only	Type 2
Nycticebus	Rods only (6)	Type 2
Galago	?	Type 2

It is apparent therefore that there is no direct correlation between the structure of the retina and the type of lateral geniculate. It is possible that the other two principal connections of the lateral geniculate play a part in fashioning its form. It has been suggested (Kappers (2) and others) that the ventral nucleus is mainly associated with the mid-brain and the dorsal nucleus with the cortex. Further investigation is however necessary to elucidate exactly the way in which the lateral geniculate contributes fibres to these two areas. These observations suggest that such an investigation in the light of the present observations would be of interest.

When we regard these Primates according to their affinity to the main stem of Primate evolution as has been interpreted by Elliot Smith (1) and others, it is apparent that those which stand nearest to the main stem have the first type of lateral geniculate, those which are more aberrant and specialised the second type. *Tupaia* and *Tarsius* are close to this stem, then come the Lorisinae of which *Perodicticus* possesses the first type. In *Galago* the presence and distribution of larger cells that are more obvious than in other specimens might be regarded as intermediate. Then more distant come *Nycticebus* and the Lemuridae. *Nyctipithecus* being a true monkey betrays this in the form of his lateral geniculate. It is interesting that the affinities of these groups determined on other grounds are confirmed by the form of the lateral geniculate.

SUMMARY

(1) Among the Primates there are two forms of the lateral geniculate: (*a*) one differentiated into a dorsal laminated nucleus and a ventral non-laminated nucleus; (*b*) a second, small dorsally, larger ventrally, but laminated throughout.

(2) The first type is the primary one; the second is the specialised aberrant form.

(3) These two types do not correspond with the two types of retinae, i.e. the rod-cone or the rod-only retina. The form of the lateral geniculate, in the

present state of knowledge does not appear to be determined by functional considerations.

(4) The distribution of the two types is in accordance with the zoological affinities of the forms studied.

BIBLIOGRAPHY

(1) Elliot Smith, G. (1908). "On the form of the Brain in the extinct Lemurs of Madagascar with some remarks on the affinities of the Indrisinae." *Trans. Zool. Soc. London*, vol. xviii, p. 163.

(2) Kappers, A. and Fortuyn, D. (1921). *Vergleichende Anatomie des Nervensystems.* Haarlem. Bd. ii, S. 897.

(3) Le Gros Clark, W. E. (1924). "On the Brain of the Tree Shrew (Tupaia minor)." *Proc. Zool. Soc. London*, p. 1053.

(4) Weber, M. (1904). *Die Säugetiere.* Jena. p. 742.

(5) Woollard, H. H. (1926). "Notes on the Retina and the Lateral Geniculate Body in Tupaia, Tarsius, Nycticebus and Hapale." *Brain*, vol. xlix, p. 77.

(6) —— (1927). "The Retina in the Primates." *Proc. Zool. Soc. London.*

THE DEVELOPING THIRD NERVE NUCLEUS IN HUMAN EMBRYOS[1]

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ALTHOUGH a great deal of work has been published on the phylogenetic evolution of the various cell groups commonly considered to form part of the third nerve nucleus in man, there does not appear to have been any exhaustive investigation of their ontogenetic development. The present paper is an attempt to trace the changes of form which the nucleus undergoes, in human embryos, from its earliest appearance until birth. The enquiry has served both to bring out two points of interest with regard to the ontogeny and to add a possible further item of evidence anent the vexed question of the localisation of function in the various cell groups which make up the nucleus. In the first place it becomes obvious that differentiation of shape of the nucleus occurs very much earlier than was previously thought, while one also sees that the ontogenetic changes of form do not correspond in sequence, as is usually stated, with the generally assumed phylogeny. The evidence *re* localisation of function is concerned with the question of the association of the Edinger-Westphal nucleus with the movements of the pupil and of the nucleus of Perlia with convergence.

Before proceeding further in a discussion of the formation of the nucleus it is necessary to explain the nomenclature to be followed. There are many classifications of the cell groups, some based on anatomical, others on physiological observations. The latter are the more elaborate and imply the existence of anatomically separate cell groups corresponding to each of the extrinsic and intrinsic ocular muscles. It must be said at the outset that such cell groups have never been demonstrated conclusively microscopically and that in all probability they do not occur, the localisation of function being of course quite possible without them.

The three best known systems of nomenclature are those of Kappers (comparative), Perlia (anatomical) and Kahler and Pick (physiological). The relation between them can be seen from the following table:

Kappers	Perlia	Kahler and Pick
1. Dorso-lateral	Anterior dorsal Posterior dorsal	Levator palp. sup. Rectus superior Inferior oblique
2. Ventro-median	Anterior ventral Posterior ventral	Rectus internus Rectus inferior
3. Median	Perlia's nucleus	Convergence
4. Accessory	Edinger-Westphal Antero-median	Sphincter iridis Ciliary muscle

[1] Work done under a grant from the Medical Research Council.

The nomenclature of Kappers has the great advantage that it is based on phylogeny and is applicable to a large number of animals and indeed, with modifications, to all the Vertebrates (above the Cyclostomes) so far investigated. Perlia's system is essentially designed from the point of view of human structure only, while the physiological scheme has little or no anatomical corroboration. The classification of Kappers will therefore be adopted in the following description as having the widest application.

According to Kappers the phylogenesis of the various cell groups is as follows:

In the *Selachian* brain the nucleus is represented by a somewhat ill-defined group of cells lying close to the mid-line on each side between the two posterior longitudinal bundles. It is not divided into separate portions, although it is slightly curved in shape, so that the ventral end lies nearer the mid-line than the dorsal, with the result that a medial and a dorso-lateral region can be recognised. This is the simplest form of oculo-motor nucleus known (see fig. 1 *A*).

In *Ganoids* and *Teleosteans* is found the first indication of a true separation into two parts. The ventral end of the nucleus has extended medially and downwards so that its lower end is only separated from the base of the brain by the *commissura ansulata*. It is only joined to the dorsal end of the nucleus by a narrow line of cells, so that in these animals the whole nucleus can be described as consisting of two groups of cells, one, the dorsal group, lying above and slightly outside the other, the ventral group, from which it is separated by some of the fibres of the posterior longitudinal bundle (see fig. 1 *B*). The ventral group extends further caudally than the dorsal.

Among the *Reptiles* are found two types of third nerve nucleus, the first resembling in arrangement that of the Ganoids, though much more clearly differentiated, the second showing a third cell group.

The alligator (fig. 1 *C*) can be taken as an example of the first type. The two cell groups, separated by the posterior longitudinal bundle, are sharply defined and are referred to as dorso-lateral and ventro-median respectively. They end at the same level behind but the dorso-lateral extends further forwards.

The lizard *Varanus* is of the second type (fig. 1 *D*). The dorso-lateral and ventro-median groups are clearly marked and, in addition, a third group of smaller cells is present, lying above and extending slightly to the inner side of the dorso-lateral portion. This third group is known as the *accessory nucleus*. It is not found below the lizards and at its first appearance is characterised by the smallness of its cells.

In *Birds* (fig. 1 *E*) the elaboration of the nucleus has progressed much further. The ventro-median group of cells is still present, lying near the middle line, below and internal to the posterior longitudinal bundle. The dorsal group has however divided into two, a dorso-median and a dorso-lateral, lying side by side above the ventro-median group. In addition the accessory nucleus is larger. It lies above the dorso-lateral nucleus.

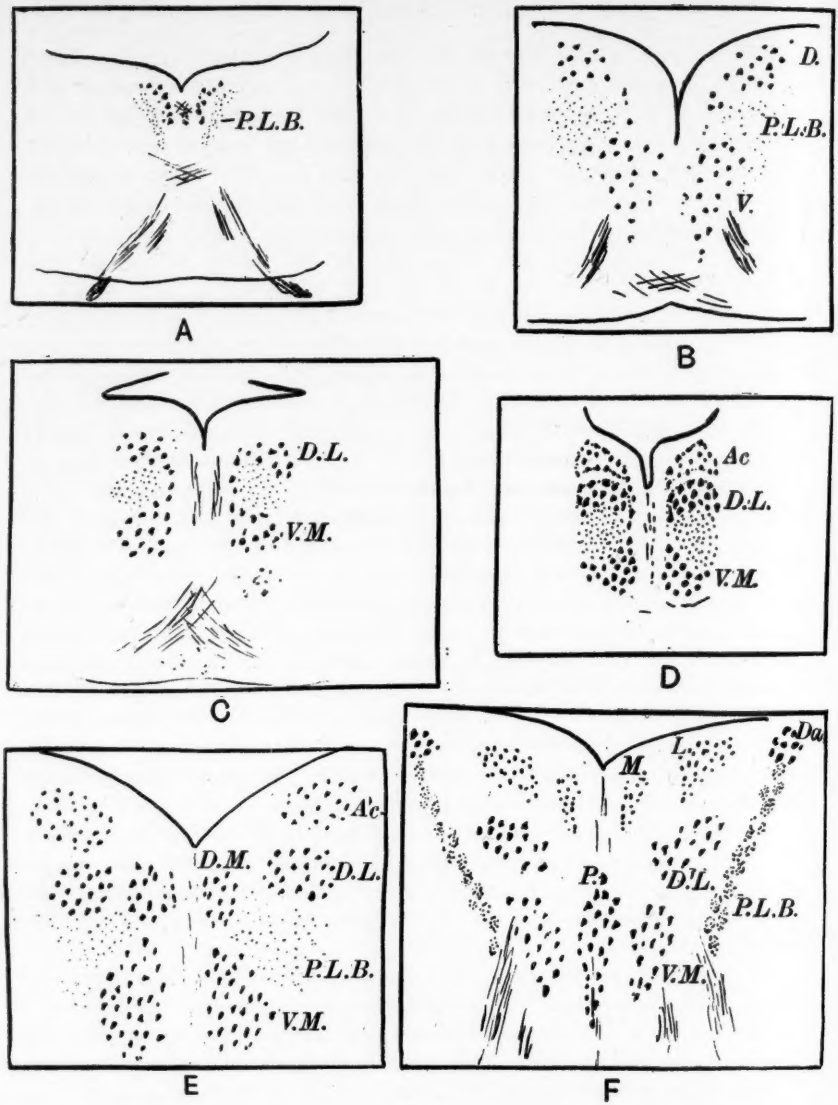

Fig. 1

A. The third nerve nucleus in a Selachian. *P.L.B* = posterior longitudinal bundle.

B. The nucleus in Ganoids and Teleosteans. *D* = dorsal nucleus; *V* = ventral nucleus.

C. The nucleus in the alligator. *D.L* = dorso-lateral and *V.M* = ventro-median group of cells.

D. The nucleus in the lizard *Varanus*. *Ac* = accessory nucleus.

E. The nucleus in the hen. *Ac* = accessory nucleus; *D.M* = dorso-median nucleus; *D.L* = dorso-lateral nucleus; *P.L.B* = posterior longitudinal bundle; *V.M* = ventro-median nucleus.

F. The nucleus in man. *Da* = nucleus of Darkschewitsch; *M* = median part and *L* = lateral part of accessory nucleus; *D.L* = dorso-lateral main nucleus; *V.M* = ventro-median main nucleus; *P* = Perlia's or median nucleus.

In *Man* the nucleus has reached its greatest known complexity (fig. 1 *F*). The ventro-median nuclei are present but are separated from each other in the anterior third of the nucleus by a mass of cells lying in the middle line (the median nucleus of Perlia). The dorso-lateral nuclei lie above the ventro-median and above them again lies the small-celled accessory nucleus, now divided into a medial and a lateral portion. The lateral portion is the nucleus of Edinger-Westphal, the medial portion is sometimes known as the antero-median nucleus. As they are both composed of the same type of cell it is better to consider them both as parts of the accessory nucleus. Yet another cell group, the nucleus of Darkschewitsch, lying above the posterior longitudinal bundle outside the accessory nucleus, is sometimes considered, but not by Kappers, as part of the third nucleus in man.

Such is the usually accepted phylogenetic history of the third nerve nucleus. Of its ontogeny little is known. Kappers states that the last group to appear in phylogeny, namely the accessory or Edinger-Westphal nucleus, is also the last to differentiate in the human foetus. According to both Kappers and Tsuchida a four to five months human foetus shows well-developed dorso-lateral and ventro-median cell groups but no median or accessory nuclei. At seven months, according to Kappers, the median nucleus is present and the accessory nucleus (lateral part) just beginning. Tsuchida states that the median and accessory nuclei do not appear until after the seventh month.

Tsuchida's work is open to one criticism. He confined his observations to material in the latter half of foetal life only, when the cells are always difficult to see, those of the accessory nucleus being particularly so, since they usually fail to take the stain. It is probable that had he examined earlier material he would have found that differentiation actually occurs and is easily visible at a much earlier date than he assigned to it.

The present series of specimens begins with a human embryo of 25 mm. I am aware that the position of the nucleus can be recognised by downgrowth of neuroblasts in the corresponding neuromere at a much earlier age, but it is only at about 25 mm. that these cells form a well-defined group. In the 25 mm. embryo examined, on either side of the median line of the floor of the aqueduct of Sylvius, can be seen a group of closely aggregated cells, still directly continuous with the ependymal lining of the canal and not differentiated. The area is indefinite in extent, fading into the surrounding brain substance, but in its most marked portion the grouping is quite definite and has the appearance seen in fig. 2.

At no part of the nucleus is there any trace of a connection of these cell groups across the mid-line.

This stage, in which the nucleus consists of two single groups of cells lying beneath the floor of the aqueduct of Sylvius on either side of the middle line and having no median connection, corresponds with the condition of the adult nucleus in Selachians as described by Kappers.

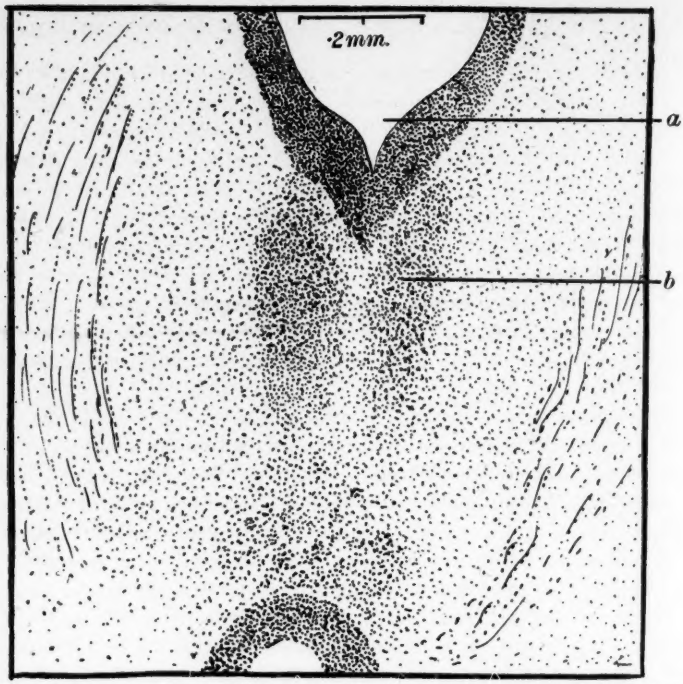

Fig. 2[1]. Horizontal section through third nerve nucleus in 25 mm. human embryo. The orientation of the brain is similar to that in fig. 3. *a* = aqueduct of Sylvius; *b* = nucleus.

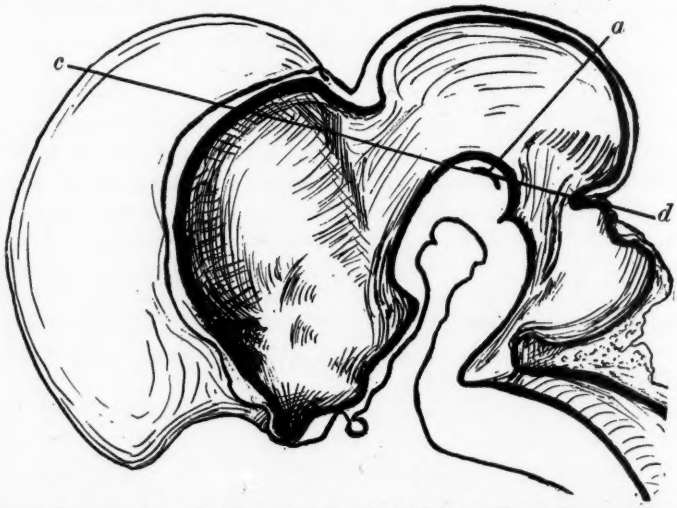

Fig. 3. Reconstruction of median sagittal section of brain of 35 mm. human embryo (after Frazer). *a* = nucleus. The line *cd* indicates the plane of section.

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The next stage to be described in the development of the nucleus is that found in a 35 mm. embryo, the appearance of whose brain is shown in fig. 3.

Fig. 4 is a drawing of a horizontal section through the nucleus which can be seen in fig. 3. It will be seen by comparison with fig. 2 that a marked change has occurred in the nucleus. The cells composing it now show the characters of differentiating neuroblasts. They are larger, have more clear protoplasm surrounding the nucleus, and the chromatin net shows a more open mesh than in the previous stage. This change renders the nucleus much more sharply

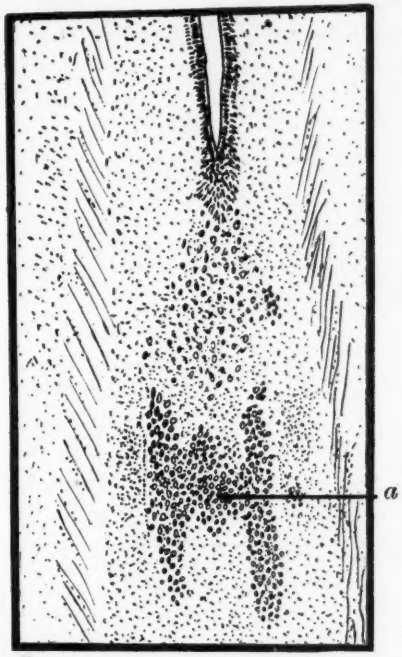

Fig. 4. Horizontal section of third nerve nucleus of 35 mm. human embryo, along the line *cd* in fig. 3. *a* = median nucleus of Perlia.

defined from the surrounding brain tissue and allows one to make out its limits with much more certainty. It will be seen that a new element has been introduced, namely, an exactly median group of cells, which connects the two lateral portions seen in fig. 2. This is the first appearance of Perlia's median group of cells. It seems to have been formed by an extension and coalescence across the middle line of the two lateral groups seen in the 25 mm. stage, since, at its earliest appearance, it is continuous with them, and in its later stages appears successively more distinct and separate. On either side of the main lateral cell groups and external to them can be seen two other small cell groups. These are more marked in sections higher than the one shown, and

can be recognised extending upwards (dorsalwards) above the upper surface of the larger cell groups. They form a narrow column of cells apparently extending in an upward and outward (dorso-lateral) direction from the main lateral masses, and, like the central mass, are connected with and apparently arise from them. Their upper limits are very ill defined. Their extent and relations are shown in figs. 5 and 6.

Fig. 5 shows a reconstruction of the nucleus seen from above. It will be noted that three definite cell groups can now be recognised, though they are at this stage all connected. A median group is connected on either side with a large group of cells from which a narrow column is growing upwards and

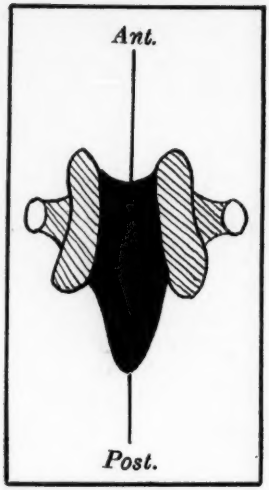

Fig. 5. Reconstruction of third nerve nucleus of 35 mm. human embryo seen from above.

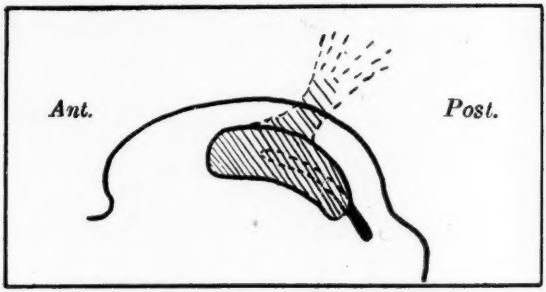

Fig. 6. Reconstruction of third nerve nucleus of 35 mm. human embryo seen from the left side. Black portion = median nucleus; lined portion = ventro-median cell group.

outwards in a dorso-lateral direction. It will be seen that the median nucleus extends beyond the lateral groups posteriorly, but does not come up as far as their anterior ends. The dorso-lateral groups are anterior to the centre of the whole nucleus. We can now, therefore, recognise the three main groups described by Kappers—a ventro-median lying alongside the middle line, a dorso-lateral extending upwards outside this, and a median uniting the two ventro-median groups. We have seen that in phylogeny the first definite indication of a division into a dorso-lateral and a ventro-median group is found in the Ganoids and Teleosteans. In them the ventro-median group is the larger, and lies in relation with the lower part of the side wall of the cleft at the bottom of the aqueduct. It is separated from the dorso-lateral part by the fibres of the posterior longitudinal bundle. The dorso-lateral part does

not extend so far posteriorly as the ventro-median. This arrangement is similar to that found in the 35 mm. embryo, except that in the human subject a median nucleus is present connecting the two ventro-median portions. The median nucleus of the 35 mm. human embryo is a simple connection and shows no forward prolongation as it does later. There is so far no trace of any cell group lying alongside the mid-line in front of the central connection and internal to the dorso-lateral and ventro-median groups, i.e. in the situation of the accessory nucleus.

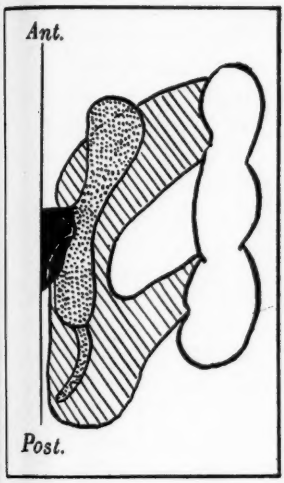

Fig. 7. Reconstruction of third nerve nucleus of 48 mm. human embryo seen from above. Black portion = median nucleus; lined portion = ventro-median cell group; dotted portion = accessory nucleus. Dorso-lateral nucleus not shaded.

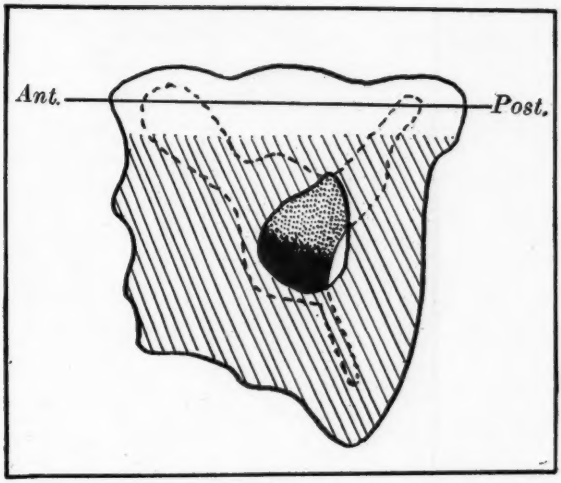

Fig. 8. Reconstruction of third nerve nucleus of 48 mm. human embryo seen from the left side. For explanation of parts see previous figure.

The next stage for consideration is the 48 mm. In the specimen I examined the various cell groups showed a uniform staining and the cells were all similar in appearance. The cell groups were easy to recognise as the specimen was darkly stained, and at this early stage the histological structure of the central nervous system is always more clearly seen than in older specimens. This probably explains the failure of Tsuchida to find the Edinger-Westphal nucleus in a five months' foetus, since the nucleus at its first appearance resembles the rest of the nucleus of the third, while, when it differentiates it becomes fainter and fainter and the cells further apart, so that it is less easy to see in the adult than in the 48 mm. embryo. The following changes (see

figs. 7, 8 and 9) have occurred: the *dorso-lateral* group has extended antero-posteriorly and now equals the ventro-median in length. It still retains its continuity with the ventro-median group at its anterior and posterior extremities, but in its middle part it is separate. The anterior part of the *ventro-median* group is on a slightly higher level than the posterior (i.e. nearer the level of the floor of the aqueduct).

The *median* nucleus has lost its continuity with the ventro-median group. It is actually larger, but not relatively so, since the ventro-median group has

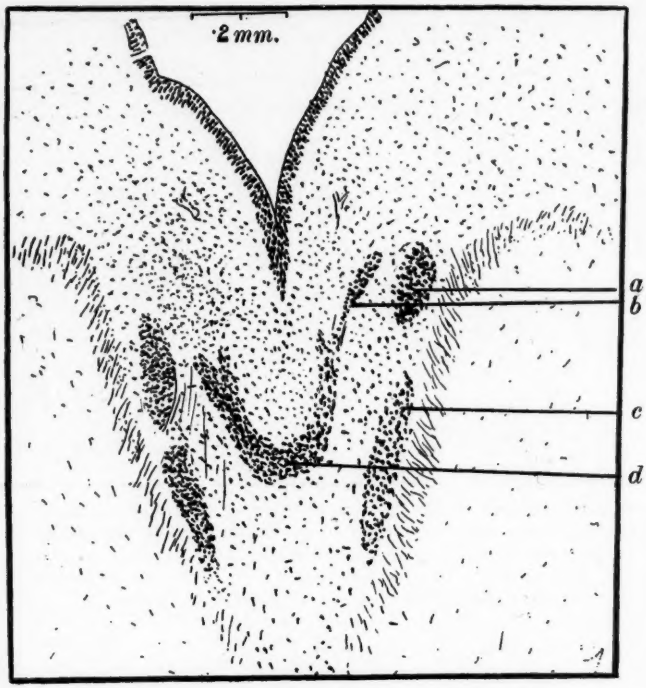

Fig. 9. Transverse section through third nerve nucleus of 48 mm. human embryo. a = dorso-lateral cell group; b = accessory cell group; c = ventro-median cell group; d = median cell group.

extended more rapidly, and now reaches further back than the median nucleus—the reverse of the 35 mm. stage. The most marked change, however, is in the form of the median group. This shows two large outgrowths, one anterior and one posterior. They will be referred to as the anterior and posterior portions of the accessory nucleus. The anterior has a blunt rounded end which extends forwards and lies beside the mid-line, internal to and above the anterior division of the ventro-median group. The posterior is shorter and passes a little backwards from the median nucleus and then extends in

two thin processes upwards and downwards, the upper one lying internal to the posterior part of the dorso-lateral group.

Fig. 7 shows the appearance from above, fig. 8 from the side. Fig. 9 shows a transverse section through the middle of the third nerve nucleus.

The four cell groups recognised by Kappers are now present though they are as yet interconnected. The dorso-lateral group is connected in parts with the ventro-median, while the accessory nucleus is present as an outgrowth from the median nucleus and shows no distinctive characters, being only recognisable from its position.

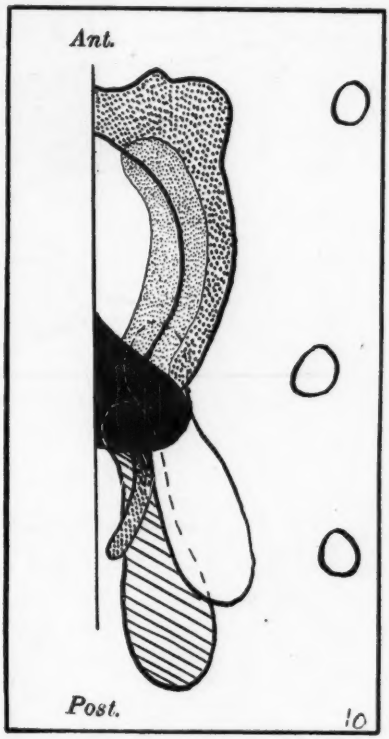

Fig. 10. Reconstruction of right half of third nerve nucleus of 75 mm. human foetus, seen from above. Shading as before. The more finely dotted portion represents the differentiated portion of the accessory nucleus.

A further differentiation has occurred in the 75 mm. foetus next examined. In the first place the *dorso-lateral* cell group has completely separated from the *ventro-median*. It lies above it and extends slightly in front of it (figs. 10, 11 and 12).

The *median nucleus* has also grown forwards in the mid-line and ends in a sharp point. This has been described by Perlia and has been seen in anthropoid apes, but is not present in the lower forms.

The *accessory* nucleus extends further forwards, curving towards the middle line, so that, just in front of the median nucleus, and also just short of its anterior end, there is a small area where it meets its fellow of the opposite side. This joining of the anterior portions of the accessory nuclei across the middle line is of interest, as, though it only occurs as a secondary and transient stage in man, it has been decribed as occurring in the adult chimpanzee (Brouwer), while in certain animals which possess an accessory nucleus, but no median nucleus, the accessory nuclei are fused (e.g. Rodents, Edentates, Marsupials).

The posterior portion of the accessory nucleus still blends with the median nucleus and extends backwards from this, dividing into an upper and a lower tongue. These are not so long nor so marked as before (at 48 mm.). The most important change, however, at this stage is that the cells lying on the upper aspect of the middle portion of the accessory nucleus (and presumably part

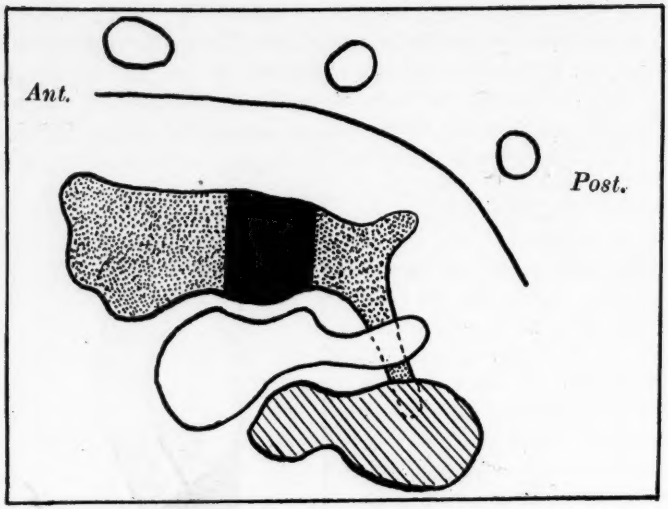

Fig. 11. Third nerve nucleus of 75 mm. human foetus seen from left side.

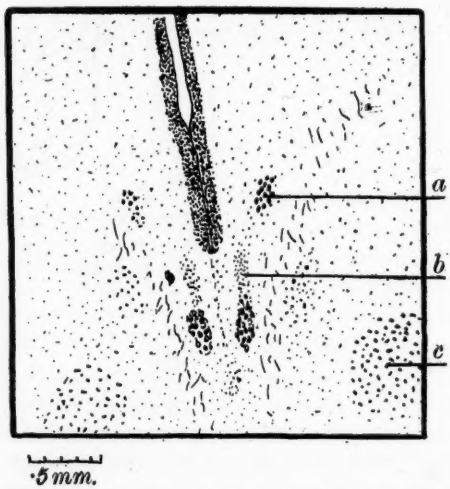

Fig. 12. Transverse section through third nerve nucleus of 75 mm. human foetus passing through anterior end of nucleus. *a* = nucleus of Darkschewitsch; *b* = nucleus of Edinger-Westphal; *c* = nucleus ruber.

of this) are now beginning to take on the adult characteristics of the cells of the Edinger-Westphal and antero-median nuclei, namely, they are smaller and the nucleus appears less deeply stained. Therefore at this stage a definite Edinger-Westphal nucleus of the adult type can be seen, though the mass of undifferentiated neuroblasts which form it had already budded out from the median nucleus by the 48 mm. stage (see figs. 10, 11, 12).

In this embryo three cell groups can be recognised lying dorso-lateral again to the dorso-lateral nucleus, in the positions indicated in figs. 10 and 11. The anterior one can be recognised as the nucleus of Darkschewitsch (*a* in fig. 12), the middle one is probably the interstitial nucleus of Cajal, which in the adult is almost continuous with Darkschewitsch, lying among the fibres of the posterior longitudinal bundle immediately posterior to it. The posterior one cannot with certainty be named at present. These three cell groups are all interconnected, and appear rather in the nature of localised thickenings in a continuous cell column than as three perfectly separated nuclei.

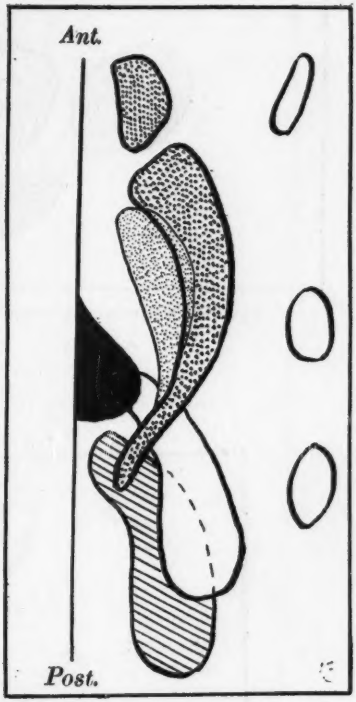

Fig. 13. Reconstruction of third nerve nucleus (right side) of 100 mm. human foetus seen from above.

In a 100 mm. foetus the main differences from the 75 mm. stage are in the direction of greater separation of the cell groups from each other. The *dorso-lateral* and *ventro-median* groups are distinct as in the 75 mm. specimen, and occupy the same positions.

The *median* nucleus with its anterior prolongation has almost completely separated from the accessory nucleus.

The *accessory nucleus* has now divided into two, an antero-median group corresponding to the portion which was fused across the mid-line in the 75 mm., and a posterior or nucleus of Edinger-Westphal. The antero-median group no longer meets its fellow in the mid-line. It does not yet show the differentiation into small cells.

The posterior part or Edinger-Westphal nucleus is only connected by a few scattered cells with the median nucleus. The cells on its upper and inner side are small and faintly stained. The upper prolongation or tongue can just be distinguished in a lateral view (fig. 14). The main trend of the nucleus, however, is in a curve concave towards the median nucleus, and with a sort

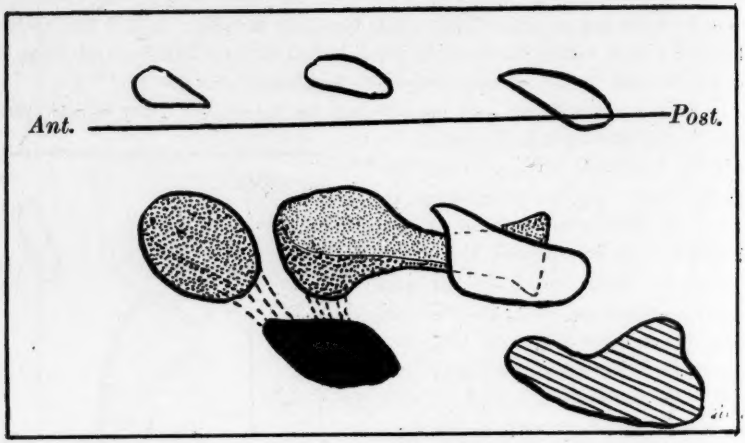

Fig. 14. Third nerve nucleus of 100 mm. human foetus seen from left side.

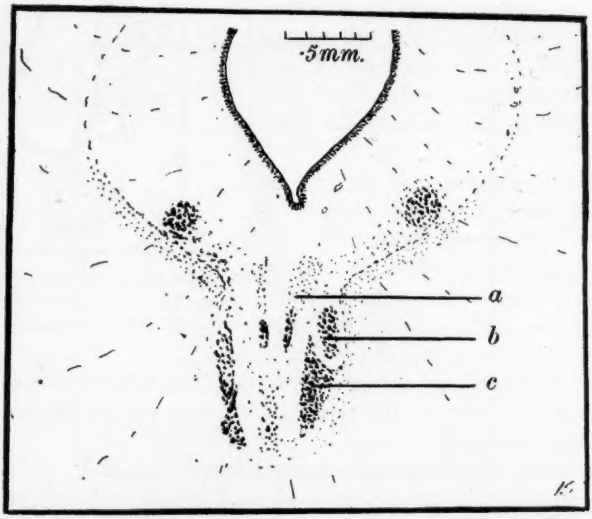

Fig. 15. Transverse section through third nerve nucleus of four months' human foetus (100 mm.). *a* = Edinger-Westphal nucleus; *b* = dorso-lateral part of main nucleus; *c* = ventro-median part of main nucleus.

of tail passing downwards and backwards in front of and internal to the ventro-median nuclei and behind and external to the median. This corresponds to the situation of the Edinger-Westphal nucleus in Perlia's well-known diagram.

As in the 75 mm. embryo, the cell column with three thickenings, of which the anterior one is the nucleus of Darkschewitsch, can be seen dorso-lateral to the main nucleus.

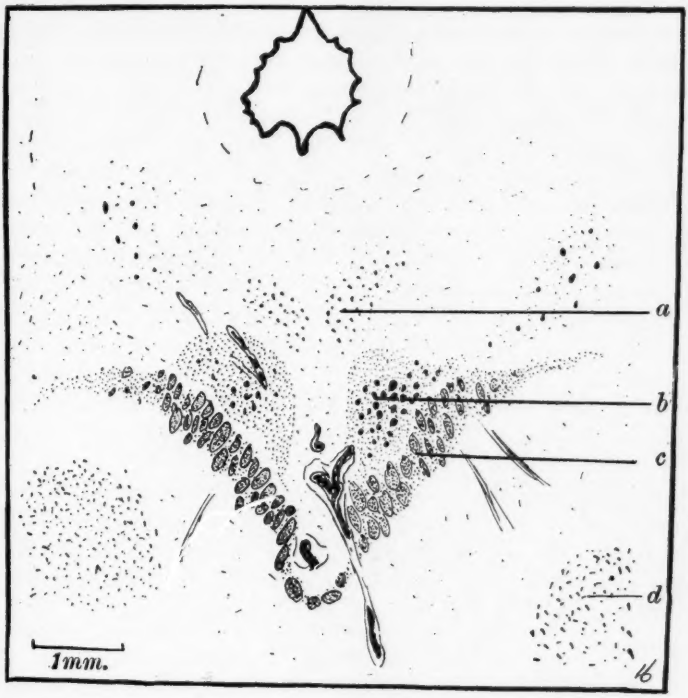

Fig. 16. Transverse section through third nerve nucleus of full term foetus. a = Edinger-Westphal nucleus; b = main nucleus; c = posterior longitudinal bundle; d = nucleus ruber.

Fig. 15 is a section through the Edinger-Westphal portion of the accessory nucleus just in front of the median nucleus, showing the differentiation of the upper part of it.

Fig. 16 is a section through the Edinger-Westphal nucleus in a full term brain showing the differentiation now complete.

From the examination of the foregoing stages it is obvious that the ontogenetic development does not follow the assumed phylogeny. It differs from this in one important particular, namely, the appearance of the median nucleus

before the accessory. The most probable explanation for this apparent discrepancy may be found in a consideration of the function of the various nuclei. It has been suggested by many observers (Hensen, Volkers, Kahler and Pick, Bruce, Westphal, Brouwer) that the accessory nucleus is concerned with the innervation of the sphincter iridis and the median nucleus with the act of convergence. If this is the case the reversal of the appearances of these two nuclei in human ontogeny may be simply an expression of the correlation of the development of an organ with the development of its nerve supply. Suppose that the median nucleus is concerned with convergence. It appears between 25 and 35 mm. and correlated with this is the fact that the maximum alteration of the optic axes in human embryos (i.e. from 120° to 72°) has also occurred by the 40 mm. stage. The peripheral mechanism of convergence is therefore developing *pari passu* with the nucleus and both are completed together. The peripheral mechanism for the light reaction does not however begin to develop until after the maximum alteration in the optic axes has already occurred. The forward growth of the margin of the optic cup to form the ectodermal portion of the iris from which the sphincter pupillae differentiates does not commence until the 48 mm. stage, at which time, as we have seen, an undifferentiated outgrowth from the main mass of the third nerve nucleus can be seen in the situation of the future nucleus accessorius. The cells forming this outgrowth differentiate slowly so that by the fifth month it is showing adult characters over its major portion. At the same time the sphincter pupillae has differentiated from the margin of the optic cup, though it is not yet vascularised.

There is therefore the possibility that this apparent reversal in order of development of the various parts of the nucleus in human embryos may be correlated with the late development of the sphincter pupillae, and may therefore constitute a further point in the evidence in favour of the connection of the accessory nucleus with the intrinsic eye muscles.

REFERENCES

Brouwer, B. (1918). "Klinisch-anatomische Untersuchungen über den Oculomotoriuskern." *Zeitsch. f. d. gesell. Neurologie u. Psychiatrie*, Bd. XL, S. 152.

Bruce, A. (1889). *Proc. Roy. Soc. Edin.* vol. XVII, p. 168.

Hensen and Volkers (1898). *Graefe's Archiv*, Bd. XXIV, S. 1.

Kahler and Pick (1881). *Prag. Zeitschr. für Augenheilk.* Bd. II, S. 30.

Kappers, A. (1920). *Vergleichende Anatomie des Nervensystems.* Haarlem.

Paton, L. and Mann, I. C. (1925). *Trans. Ophth. Soc.* vol. XLV.

Tsuchida (1906). "Über die Ursprungskerne der Augenbewegungsnerven." *Arbeiten aus dem Hirnanatomischen Institut in Zürich*, Heft 2, Wiesbaden.

THE PROBLEM OF THE INNERVATION OF THE DENTINE

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I. INTRODUCTION

The question as to whether the dentine is supplied with nerve fibres is of great importance to the dental surgeon. In his clinical work he is continually treating carious teeth, in which the dentine is extremely sensitive to pain, and in his efforts to relieve it he is hampered by having no definite information as to its etiology.

This problem has interested workers for many years, and the literature is fairly extensive. In this communication an elaborate description of this literature will not be given, as it has been frequently reviewed in the past. Only the more important papers will be discussed, and several hypotheses, which are now of purely historical interest, will not be considered.

When the more modern views are studied it will be found that they fall into two distinct groups. The members of the first believe that the nerve fibres of the tooth pulp end around the odontoblast cells; those of the second group claim to have traced the nerve fibres into the dentinal tubules.

Retzius, who was one of the earlier advocates of the hypothesis that the fibres terminated among the odontoblasts, published a series of papers (33, 34, 35), in which he described the course of the dentinal nerves in the different classes of the Vertebrates. In every case he used Golgi's stain. In the Fish he found that the nerve fibres branched repeatedly, and finally invested the inner surface of the dentine, giving off free-ending lateral branches. The nerves did not appear to extend to the tip of the pulp. In the Amphibians the arrangement was similar to that in the Fish, except that fibres in the periodontal membrane could be traced as far as the epithelium of the mouth. In the Reptiles fine nerve fibres were given off from the nerve trunks in the middle of the pulp, and ran to its sides and top. They passed through the odontoblast layer and ended in the inner surface of the dentine in knotty points. In the Mammals Retzius had great difficulty in following the nerves to their destination, but finally in the tooth of a young mouse he traced them to their termination, which was similar to that of the Reptiles except that on arriving at the dentinal surface, they ran tangentially for a short distance.

Huber (16) appears to have been more successful with mammalian teeth, for which purpose he used the pulps of rabbits' teeth stained with Ehrlich's *intra-vitam* methylene blue. He states that when the nerves approach the

surface of the pulp they lose their medullary sheaths, divide repeatedly, and form a network under the odontoblasts, but the individual fibres do not anastomose. From this network fibres pass between the odontoblasts to end in the manner described by Retzius.

Professor Hopewell-Smith, the leading British advocate of this school, published, as far back as 1894 (8), a paper in which he put forward the idea, that the dentine is formed by small round cells, and not by the odontoblasts, which, he considered, were solely for the transmission of nervous impulses. At that time he was unable to establish any connection between the nerve fibres and the odontoblasts. In 1903 (9) he was able to describe such a connection, for he says that the nerve fibres of the pulp "terminate in a basket-work of varicose fibres, embracing and often closely attached to the cell walls of the individual odontoblasts." Since that time Hopewell-Smith has apparently seen no reason to alter his views on this subject, and has been a strong antagonist of the views of Mummery, to be described later, as can be seen by consulting different papers written by him during the last few years (10–14). Other authorities who consider that the nerve fibres end in association with the odontoblasts are Hoehl (7), Walkoff (38, 39), Fischer (4), Noyes (32), and Gysi (6).

The hypothesis that the nerve fibres actually enter the dentine has had numerous adherents since the time of Boll (1), in 1868; among the more prominent are Dependorf, Mummery, and Carol Montfort.

Dependorf (2, 3), found that the non-medullated nerves formed a sub-odontoblastic plexus, and then passed through the odontoblasts in the most diverse manner, giving off lateral branches to the cells. Near the dentinal margin their course became straighter. Using Lowitz's, Bielschowski's and Held's stains, he found two types of nerve fibres in the dentine; one group in the dentinal tubes had club-shaped endings, the other in the ground substance terminated in a fine plexus at the dentino-cemental margin.

The late Mr J. Howard Mummery, up to the time of his death in the autumn of 1926, was the leading British supporter of the view that the dentine contained nerve fibres. Towards the end of the last century he stained some teeth with iron and tannin, and was able to trace fibres which appeared to be nerves to the dentinal margin, but could not definitely satisfy himself that they entered the dentine (23, 37). In 1910 he re-examined these sections and found that he could now follow the fibres into the dentine (23). A little later he published two papers (24, 26) containing the results of some experiments in which he had stained sections of teeth with Beckwith's gold chloride; his conclusions were as follows: "The nerves of the dental pulp lose their medullary sheaths, and neurolemma just beneath the odontoblast layer, and are seen to form an intricate plexus of neuro-fibrils in this situation, the plexus of Raschkow; from this plexus they pass in approximately straight lines between and around the odontoblast cells and form another much narrower plexus at the inner margin of the dentine, which I have called the 'marginal plexus.'

They very closely envelop the cells and the dentinal fibrils and enter the dentine in company with the latter. They can be traced as fine beaded fibrils all along the tubes and their very numerous branches, and are seen to terminate in the fine ramifications of the dentinal tubes beneath the enamel and cementum."

In a short supplementary paper (25) he announced that he was now able to trace the nerve fibres from the nerve trunk to the dentine without interruption. In 1916 he had some doubts as to the existence of the marginal plexus, as he then stated (27) that it is very small, being formed only by a few of the fibrillae, and that in the most completely reduced specimens nearly all the main fibrils pass directly to the dentine.

In 1919 (28, 29) Mummery found structures interposed in the course of the nerves, which he considered were nerve cells. These were placed in a row along the bases of the odontoblast cells. Fig. 1, which is reproduced from Mummery's *Microscopic Anatomy of the Teeth*, p. 22, shows the connection of the cells with the nerve fibres. There is one point mentioned by the author, which this diagram does not illustrate, which is that the peripheral process of the nerves have a markedly wavy cork-screw-like course. It will be noticed that in the diagram there is no indication of the "marginal plexus," which he described in his earlier papers. Mummery's reasons for omitting it are as follows: "Small enlargements or nodes are seen upon the fibres distributed around the odontoblasts, but are not present in the distal or dental process. It is these enlargements that were considered by Huber, Guido Fischer and others to form the terminations of the nerve fibres of the pulps and which are similar to those shown by Retzius in the mouse, and in fish and reptiles. It is these strongly beaded fibres which I first described as the marginal plexus, but although my first preparations appeared to indicate that the neurofibrils which pass into the dentinal tubes arise from this plexus, the later ones show that this is not the case, for these fibres pass direct to the dentine as the distal processes of the nerve-end cell with which they are continuous. What I had formerly described as the marginal plexus is evidently a portion of the network of fibres surrounding the odontoblasts and extending to the dentine margin; it is derived from the dendritic processes of the nerve cells."

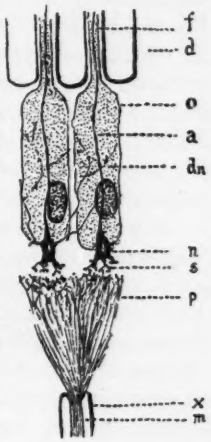

Fig. 1.

The work of Mummery has been dealt with rather fully, as it formed the starting-point of the investigation, a description of which is contained in this paper.

Carol Montfort in 1914 apparently published in a Spanish dental journal, which I have been unable to obtain, the results of some experiments with Bielschowski's stain, by which means he claims to have found nerve cells

within the dental pulp. In 1920 (20) and 1923 (21) he published two further papers in the *Dental Cosmos*, in which he described an elaborate system of nerves in the pulp cavity.

It consists of

(1) Non-myelinated nerve fibres which end in knotty expansions around the odontoblasts.

(2) Medullated nerves which lose their myelin and end in the plexus of Raschkow.

(3) Sub-dentinal nerve cells, which have two dendrons entering the dentinal tubes.

(4) Nerve cells in the central part of the pulp.

He also claims to have found neuroblasts in the dental follicules of the new-born cat.

It should be noted that Montfort's nerve cells correspond in no way to those of Mummery, which as we saw in fig. 1 had only one process running to the dentine, and which in form, if not in function, resembles an axon fibre.

A serious criticism of Montfort's work is that he relied mainly on Bielschowski's stain, which is uncertain in its actions, so that many of the cells which he thought were of nervous origin were probably only impregnated connective tissue cells.

Among other workers who consider that the dentine is innervated are Fritsch (5), Morgenstern (22), Latham (18), Law (19), Römer (36) and Welling (40).

It will be noticed, from this review of the literature, that those workers who believe that the nerve fibres enter the dentine have given such differing accounts of the arrangement and course of these fibres that it is impossible to reconcile their results with each other. On the other hand, there is no insurmountable difference in the description given by those who consider that the nerve fibres end around the odontoblast cells. This conclusion, however, at least implies that sensory stimuli from the dentine are in the first place conducted along the dentinal fibres of the odontoblasts, and Hopewell-Smith advocated this view. There is a difficulty in accepting such a hypothesis, as the odontoblasts are of mesodermic origin.

From this summary of the results of earlier workers it will be seen that our knowledge of the termination of the dentinal nerves is unsatisfactory. It therefore appeared desirable that a further investigation should be carried out on the subject and with this aim in view I repeated the work of Mummery. The reasons for this choice were:

(1) It was the latest work on the subject and had been very favourably received by a large number of British dental histologists. Professor Hopewell-Smith however had strongly dissented, and written several papers stating his belief that Mummery's conclusions were unsound.

(2) Mummery's description of a special end neurone at the end of a somatic sensory nerve, differed entirely from the conditions found anywhere else in the body. It might be considered that they were end organs of some de-

scription, but during an investigation into the tactile sensibility of the teeth, I found evidence, which has not yet been published, which suggested that the fibres of the pulp carried only painful stimuli, and such nerves are believed to end as branching fibrils.

(3) Mummery's papers were easily accessible and were freely illustrated with very excellent microphotographs, which assisted greatly in comparing his results with my own.

II. HISTOLOGICAL OBSERVATIONS

In this portion of the investigation, the various methods employed by Mummery were carefully followed. In his earlier work in which he claimed to have traced the course of the nerve fibres into the dentine, he used freshly extracted normal human teeth (removed mainly from children who were under orthodontic treatment). These he divided transversely into two parts and then fixed them in formol and afterwards decalcified them in 30 per cent. formic acid. They were cut into sections with a freezing microtome, and finally stained with gold chloride by Beckwith's method. A full account of the technique is given in his original paper(24). As it was by means of this technique that Mummery claimed to have discovered the nerve fibres, and did not advance the hypothesis of the presence of nerve cells in the pulp until a later date, it was considered better to deal with the fibres in the first place and leave the problem of the cells until a later date.

Sections stained by the above method were made and examined. They were found to show, very clearly, the fibres described by Mummery, for these stood out as black lines against the general red background of the pulp. About 250 sections from human teeth were prepared by this method, and in the great majority of cases the fibres were seen.

Fig. 2 illustrates a transverse section from the root of a bicuspid of a female aged 42 and was one of the earliest preparations made. It demonstrates several of the characteristics of these fibres which Mummery noted and described. They run through the odontoblast zone in a direction more or less parallel to the long axis of those cells. In the actual section the odontoblasts are not nearly as conspicuous as in the photograph and are stained faintly pink. The beaded appearance of some of the fibres will be noticed; in the actual specimen a large number of the fibres exhibit this appearance if examined with a sufficiently high magnification. Mummery attached considerable importance to this beading, as being characteristic of non-myelinated nerves. It will be seen that some of the fibres have the markedly wavy course described by their discoverer, and that most of them appear to begin immediately internal to the odontoblasts in the region of Raschkow's plexus, which is not clearly stained in this preparation. Some of the fibres can be traced inwards towards the centre of the pulp; Mummery also noted this, and claimed to have followed some of the fibres to their origin from a medullated nerve; in

none of my specimens was it possible to establish such a connection. At their distal extremity the fibres ended suddenly at the edge of the dentine as if they entered it, but in this specimen none of them could be traced actually into that tissue. The fibres do not give off side branches to the odontoblasts and in some of Mummery's photographs the same lack of branching will be noticed.

Fig. 3 represents a longitudinal section from the crown of an incisor from a female aged 26. In this section the fibres pass through the odontoblast layer and can then be traced into the dentine.

Although the last two sections do not show the sub-odontoblastic plexus, it has been seen frequently. Another feature of the fibres of Mummery which that author noted is their elasticity. During the preparation of specimens it frequently happens that a portion of the pulp is torn away from the dentine, leaving a gap which is often bridged over by some of these fibres. These are seen to be under tension, as they are now quite straight instead of wavy, and the beaded appearance is more conspicuous than usual. The above condition has been seen quite commonly during the present research.

Teeth from the monkey, cat, dog, sheep, hedgehog, rabbit and guinea pig were treated with Beckwith's stain, and Mummery's fibres were found in every case. They showed all the characteristic features seen in man, and therefore require no further description.

The repetition of Mr Mummery's earlier work confirmed the existence of fibres which entered the dentine, and which in many of their histological characters resembled non-myelinated nerves. His statement that they were continuous with the myelinated nerves was not confirmed; neither were any structures resembling nerve cells seen. The next step therefore was to repeat his later work and employ the method of staining with which he claimed to have demonstrated these cells. The technique adapted by that author can be found in his paper on this subject(29) and need not be described in detail here. It consisted essentially of a modification of the original method, so that portions of teeth could be stained in bulk before being sectioned. The teeth were suspended in a 1 in 5000 solution of gold chloride for a week or longer and afterwards reduced in the ordinary Beckwith way.

This technique proved to be very disappointing; out of twenty-six different pieces of teeth which were treated in this way, in only five were sections found which showed the fibres definitely, and in none of these were the details as clearly seen as in those sections which had been treated with Beckwith's stain. None of them contained any structures which even resembled nerve cells.

I had some correspondence, and afterwards an interview, with Mr Mummery on this subject, and he informed me that he had experienced the same difficulty, and that by far the greater part of his preparations were failures. I gathered that only one section (which he kindly allowed me to examine, and afterwards sent on to me at Manchester for a few days) showed the cells

at all clearly. After receiving this information, I carried out some experiments, to see if any modification could be found which would make Mummery's technique more satisfactory. The results of these experiments suggested certain alterations which gave markedly improved results. The strength of the gold chloride solution was increased from 1 in 5000 to 1 in 1000, and was acidulated by the addition of four drops of concentrated hydrochloric acid to every 100 c.c. of the gold solutions. These modifications practically stopped the precipitation of the gold on to the tooth while it was being stained. The portion of tooth being stained was left in the gold solution for three weeks and afterwards treated with the ordinary Beckwith reducing reagents for the following periods:

20 per cent. sodium hydrate	1 hr.
10 per cent. potassium carbonate	24 hrs.
10 per cent. potassium iodide	24 hrs.

The specimens were then sectioned with a freezing microtome, dehydrated and mounted.

By the above technique sections were obtained which closely resembled those obtained by Beckwith's original stain. The fibres were clearly demonstrated, but no nerve cells were found in any of the three hundred sections examined.

Beckwith's and Mummery's stains and the modification of the latter, which I devised, are so closely related, that if nerve cells can be picked out by one method, they ought also to be found with the others, but in no case has this been possible, although 1034 sections were prepared and examined, which showed Mummery's fibres. As mentioned above, I have seen that investigator's preparation in which the cells were found, and after careful examination am of the opinion that they are not nerve cells. Professor Stopford has also examined this preparation, and agrees with my conclusions. As Mummery stated that very complete reduction is required to show these cells, some of the sections stained by Beckwith's method were left for several hours in potassium iodide solution, but the only results were that all the fibres of the pulp became black, and no nerve cells were found.

Other metallic impregnation methods, Bielschowski's and Nabias', were tried; when successful they gave results similar to those described above, but a very much larger proportion of failures was obtained with these stains. With Bielschowski's stain, which had been used by Carol Montfort, no structures resembling those described by that worker as nerve cells were seen.

At that stage it became clear that no further information could be expected from methods depending upon impregnation with gold or silver. They stained fibres which resembled nerves, but on account of the unreliability of these methods, in that they are liable to stain all sorts of tissues, it was impossible to say with certainty that the fibres were of nervous origin.

A variety of other stains were now tried and the results obtained are briefly described in the following paragraphs.

Van Giesen, haemalum and eosin, Weigert's resorcin fuchsin, rubin and orange G, Mallory's haematoxylin ammonium molybdate or phospho-tungstic did not stain Mummery's fibres. Nissl's stain failed to reveal any structure which resembled nerve cells.

Stroebe's stain (Mallory and Wright's *Pathological Technique*, 7th ed., p. 134) brought out a few fine blue fibres in the position usually occupied by those of Mummery, and that author considered this to be an additional argument in favour of these structures being nerves. Unfortunately the dentinal fibres and tissues of the pulp stain quite as deeply as these fibres, consequently the stain cannot be considered as specific for nerve fibres, and does not therefore give any assistance in solving the problem of the nature of Mummery's fibres.

Mallory's connective tissue stain gave interesting results. If the sections were not thoroughly washed after immersion in the aniline blue and orange G solution, the fibres of Mummery were stained dark blue. In those cases where the washing had been carried out more carefully the fibres disappeared or became so pale that it was impossible to say with certainty that they were present. It must be remembered that Mallory's stain colours connective tissue blue and nerve fibres red, so that the result obtained in this case casts grave doubt on Mummery's hypothesis that his fibres are of nervous origin.

The results of this histological investigation into the nature of Mummery's fibres may be summarised as follows: They are stained by metallic impregnation methods, but not by Mallory's nerve stains. On the other hand, they are stained by Stroebe's method, but so are the other tissues. The ordinary stains for white fibrous and elastic tissue do not seem to affect them, but with Mallory's connective tissue stain they respond like white fibrous tissue. These different results must lead to the conclusion that the nature of Mummery's fibres cannot be settled finally by purely histological approach, without the assistance of other methods of research.

III. THE RESULTS OF SECTION OF THE INFERIOR DENTAL NERVE

The account in the last section of the results obtained from different histological stains showed, that those stains left it very doubtful whether the fibres of Mummery are of nervous origin. As we have said, it seemed improbable that a definite decision, as to the nature of the fibres, would ever be arrived at by such means. It was therefore decided to attempt to elucidate the problem by the experimental method. For this purpose it was considered that the study of the effect on the pulp, of section and degeneration of one of the nerves to the teeth would be of great value, and would provide a new means of approach to this question.

The inferior dental nerve was chosen in preference to one of the superior ones, as it is more accessible, and on account of there being only one nerve on either side in the lower jaw, there is less overlapping of their areas of dis-

tribution than in the upper. There is only one objection to the use of this nerve, and that is due to the fact that the nerve on one side is believed (on clinical grounds) to extend for some distance into the opposite half of the jaw. How far this distribution is carried is at present uncertain and requires investigation, but the nerve is not believed to supply teeth farther back than the opposite canine. Consequently it seems possible to exclude fallacies due to overlap by using for examination, teeth posterior to the canine.

The experiments were performed on the cat in preference to the rabbit or guinea-pig, on account of various peculiarities in the nerve supply of these teeth, which are still being investigated, and a description of which will be published at a later date.

In carrying out the operation the line of approach selected was *via* the mouth, and in each case the left nerve was divided. Six cats in all were operated upon, two (Nos. 1 and 4) were killed on account of sepsis, No. 2 was killed at the end of a fortnight, No. 3 after three weeks and Nos. 5 and 6 after a month. In cat No. 5 it was found, post-mortem, that the nerve had not been divided, but in the other three cases the operation had been successful. In the successful cases the teeth were disposed of in the following manner. The canine and the three teeth posterior to them on each side of the lower jaw, were hardened and decalcified in the usual way, and cut into sections with the freezing microtome. These teeth were numbered 1 to 4 from before backwards. At the same time those parts of the inferior dental nerve of both sides which lay in the mandibular canals were stained with Marchi, embedded in paraffin, and cut into sections. In each case therefore the structures on the normal side could be used as controls for those on the abnormal side.

Sections from tooth No. 4 of cat No. 2 were first of all stained with haemalum and eosin, and on examination no difference could be seen in the sections from the two sides. This confirms the results of Hopff (15) who cut the inferior dental nerve in ten rabbits, and could find no structural changes in the pulp tissues after this operation. He did not however study the state of the nerves of the pulp.

The inferior dental nerves which had been stained with Marchi were now examined, and it was found that degenerative changes had occurred in each case on the affected side. No alteration had taken place in the normal nerves.

The decalcified sections were now stained in the usual way by the Beckwith method, and the results obtained in one of the teeth of cat No. 2 are shown in figs. 4 and 5 which are sections from the corresponding teeth from the opposite sides of the mouth. It will be noticed that the fibres of Mummery are present, and are equally abundant upon both sides. In fact the sections from the various teeth on the denervated side cannot be distinguished by any histological alteration from the corresponding ones on the normal side. The teeth of cats Nos. 3 and 6 were treated in the same way with Beckwith and in spite of the increased time allowed for degenerative changes to take

place, the appearance of the sections from the opposite sides of the jaw is identical. This can be seen in figs. 6 and 7 which are from the farthest back teeth of cat No. 6, in which the degenerative changes were allowed to continue for four weeks.

A few sections were treated with Bielschowski's method, but as it had been very unreliable in the earlier part of this research it was only used for one pair of teeth (No. 4 of cat No. 2). Only 12 per cent. of the sections previously stained had shown the presence of fibres, so it was considered that if fibres were found only in one or two of the sections of the denervated side the result would be satisfactory; actually the percentage on that side was better than on the normal one, being 20 per cent. to 11·4 per cent. In no case however were the fibres clearly seen.

IV. DISCUSSION

The results of these denervation experiments show that whatever else Mummery's fibres may be, they are not the terminal fibres of the dental nerve. The experiments do not rule out completely the possibility of the fibres having a nervous origin, as it could be argued that they formed part of a separate neurone, or arose from the sympathetic plexus around the inferior dental artery, which was not divided at the operation.

The validity of the first argument rests upon the hypothesis that nerve cells as described by Mummery and Carol Montfort are present in the pulp. In regard to these structures however we must recall the following facts:

(1) The above-mentioned authors have described two entirely different structures as nerves.

(2) The stains they employed are, for teeth at least, extremely unsatisfactory in their action, being liable to stain all manner of tissues.

(3) Mummery's cells do not resemble nerve cells in appearance.

(4) Throughout this research, in which a large number of sections were examined, no structures in any way resembling nerve cells were found.

(5) No such arrangement has been found at the termination of any somatic nerve.

From these facts, therefore, we can safely say that there is no evidence to support the belief that nerve cells occur in the pulps of mammalian teeth.

The question as to whether these fibres might not arise from the sympathetic plexus around the inferior dental artery is one of greater difficulty, and cannot be finally settled with the evidence at present in our possession. On account of the large number of Mummery's fibres found in each tooth it is unlikely that they arise from the periarterial plexus which must be relatively extremely small. It is also probable that the inferior dental nerve gives off branches at intervals to the plexus, and if this is the case, when that nerve is divided the plexus will be still further diminished in size. However, to settle this point finally it will be necessary to divide the artery along with

the nerve in order to exclude every source of nerve supply to the pulp. I hope to carry out this experiment during a later investigation.

The question which now arises is, what is the nature of Mummery's fibres if they are not nerves? At present it is impossible to give any definite opinion on this matter. Professor Hopewell-Smith has put forward the view that they may be the same as the fibres of Korff. v. Korff(17) in 1906 saw fibres which stained with connective tissue stains in the same position as those of Mummery, and they had the same cork-screw like appearance. They were found however only in embryonic teeth and never in fully developed ones. An attempt was made, during this investigation to find these fibres in sections taken from teeth in which Mummery's fibres had been seen in large numbers. This was unsuccessful, although the same stains as v. Korff employed were used. From these facts it seems rather difficult to believe that the fibres of Mummery and v. Korff are identical. One suggestive observation was made however: in some of the sections stained by one of the impregnation methods a piece of bone was present and Sharpey's fibres could be seen, which, although much thicker, resembled Mummery's fibres in their staining properties. It is therefore possible that there may be some morphological relationship between them.

This portion of the investigation has been confined to checking the work of those authors who believe that the dentine is innervated with fibres from the pulp and it has shown that there is at present no evidence that it obtains a somatic supply from this source. At present further work is being carried out with other methods, and will be published when they are completed.

No attempt has been made to study the nerve endings in the periodontal membrane, as the methods employed stained that tissue so densely that it was impossible to trace nerve fibres into it. It must be borne in mind however that it is possible that the dentine receives nerves from that tissue, and certain experiments which I have made on the power of teeth to locate pressure stimuli suggest that this may possibly be the case.

V. SUMMARY AND CONCLUSIONS

(1) Gold impregnation stains demonstrate fibres described by Mummery which resemble nerves in certain of their characters.

(2) Section and degeneration of the inferior dental nerve does not cause these fibres to disappear from the teeth which it supplies, consequently they are not the terminal fibres of that nerve.

(3) Nerve cells as described by Mummery and Carol Montfort are not present in the pulps of teeth, therefore the fibres of Mummery cannot be a part of an end neurone on the somatic sensory tract.

(4) Mummery's fibres may possibly arise from the periarterial plexus associated with the inferior dental artery. This is improbable, but the difficulty can only be solved by division of the artery along with the nerve.

(5) The tentative suggestion is put forward that there may be a relationship between the fibres of Mummery and those of Sharpey.

I have to acknowledge my indebtedness to Professor Stopford for many helpful suggestions. Professor Raper kindly allowed me to use the laboratory of the Physiology Department of Manchester University to carry out the nerve section experiments. The following gentlemen have supplied me with material: Messrs Campion, Fish and Matthews. Mr Gooding of the Anatomy Department has prepared the microphotographs, and I have received great assistance from my wife in preparing the paper for publication.

I have to thank the Oxford University Press for permission to use the diagram in fig. 1.

BIBLIOGRAPHY

(1) Boll, F. (1868). *Archiv für Mikroskopische Anatomie*, Bd. IV, pp. 73–87.
(2) Dependorf (1913). *Deutsche Monatschrift für Zahnheilkunde*, Bd. XXXI, S. 377–81.
(3) —— (1913). *Deutsche Monatschrift für Zahnheilkunde*, Bd. XXXI, S. 570–2.
(4) Fischer, G. (1909). *Bau und Entwickelung der Mundhohle*. Leipzig.
(5) Fritsch, C. (1914). *Arch. f. Mikros. Anat.* Bd. LXXXIV, S. 307–20.
(6) Gysi, A. (1900). *Brit. Journ. of Dental Sc.* vol. XLIII, pp. 865–8. (Extract.)
(7) Hoehl, E. (1896). *Arch. f. Anat. u. Phys.* (*Anatomie*), S. 31–54.
(8) Hopewell-Smith, A. (1894). *Trans. Odontological Soc. Gt. Brit.* n.s., vol. XXVI, pp. 9–35.
(9) —— (1903). *Histology and Patho-Histology of the Teeth*. 1st ed. London.
(10) —— (1916). *Dental Cosmos*, vol. LVIII, pp. 421–7.
(11) —— (1922–3). *Proc. Roy. Soc. Medicine*, vol. XVI, odont., pp. 58–71.
(12) —— (1924). Correspondence in *Brit. Dent. Journ.* vol. XLV, pp. 575–6.
(13) —— (1924). *Dental Cosmos*, vol. LXVI, pp. 489–506.
(14) —— (1924). *Proc. Roy. Soc. Medicine*, vol. XVII, odont., pp. 64–79.
(15) Hopff, R. J. (1924). *Compt. Rend. de la Soc. de Biol.* T. XCI, p. 25.
(16) Huber, G. C. (1898). *Dental Cosmos*, vol. XI, pp. 797–811.
(17) v. Korff, K. (1906). *Arch. f. Mikros. Anat.* Bd. LXVII, pp. 1–17.
(18) Latham, V. A. (1902). *Jour. Amer. Med. Ass.* vol. XXXIX, pp. 63–74.
(19) Law, W. J. (1907–8). *Proc. Roy. Soc. Med.* vol. I, odont., pp. 45–60.
(20) Montfort, J. Carol (1920). *Dental Cosmos*, vol. LXII, pp. 871–4.
(21) —— (1924). *Dental Cosmos*, vol. LXV, pp. 917–37.
(22) Morgenstern, M. (1896). *Arch. f. Anat. u. Phys.* (*Anatomie*), pp. 378–94.
(23) Mummery, J. Howard (1910–11). *Proc. Roy. Soc. Med.* vol. IV, odont., pp. 51–6.
(24) —— (1911–12). *Proc. Roy. Soc. Med.* vol. V, odont., pp. 166–90.
(25) —— (1912–13). *Proc. Roy. Soc. Med.* vol. VI, odont., pp. 23–6.
(26) —— (1912). *Phil. Trans. Roy. Soc.* B, vol. CCII, pp. 337–49.
(27) —— (1916). *Dental Cosmos*, vol. LVIII, pp. 258–69.
(28) —— (1919). *Microscopic Anatomy of the Teeth*. London.
(29) —— (1920). *Phil. Trans. Roy. Soc.* B, vol. CCIX, pp. 321–9.
(30) —— (1924). *Brit. Dental Journ.* vol. XLV, pp. 303–5.
(31) —— (1924). *Proc. Roy. Soc. Med.* vol. XVII, odont., pp. 35–47.
(32) Noyes, F. B. (1921). *Text Book of Dental Histology and Embryology*. 3rd ed. p. 177.
(33) Retzius, G. (1892). *Biolog. Untersuch.* Bd. IV, S. 65–6.
(34) —— (1893). *Biolog. Untersuch.* Bd. V, S. 40–1.
(35) —— (1894). *Biolog. Untersuch.* Bd. VI, S. 64.
(36) Römer, O. (1909). *Atlas der pathologischen Anatomischen Veranderungen den Zahnpulpa*. Freiburg. Teil I, pp. 15–16, and plate 12.

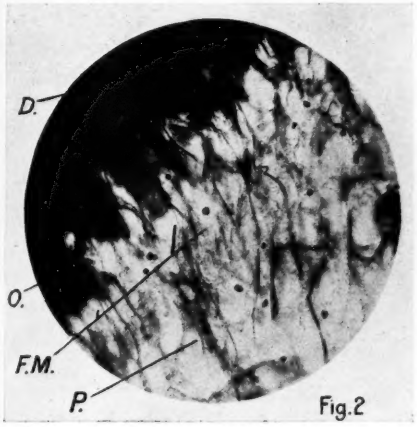

Fig.2

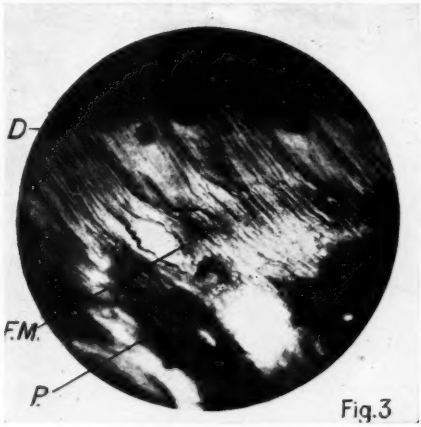

Fig.3

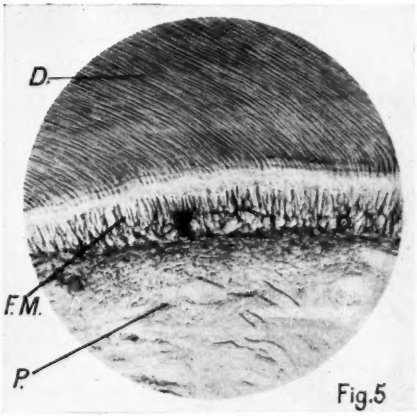

Fig.5

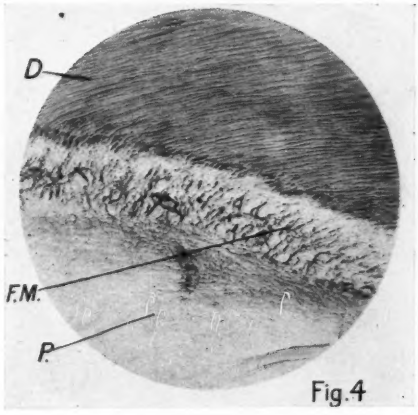

Fig.4

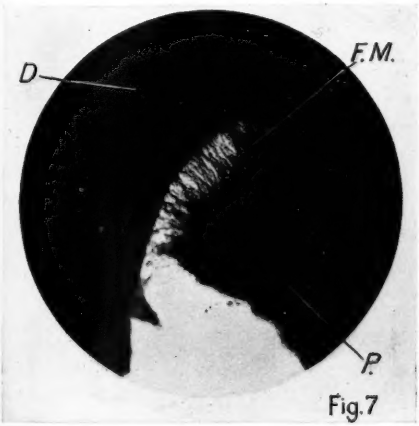

Fig.7

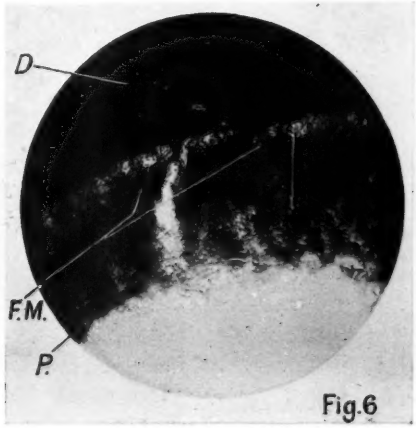

Fig.6

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(37) TOMES, C. S. (1908). *Manual of Dental Anatomy.* 6th ed. London. p. 98.
(38) WALKOFF, O. (1899). *Correspond-Bt. f. Zahnärzte.* Bd. XXVII, S. 103–9.
(39) —— (1923). *Deut. Zahnheilkunde,* Heft 60.
(40) WELLING, A. W. (1923). *A Text Book of Dental Anatomy and Physiology.* London: Humfrey and Welling, pp. 133–41.

INDEX OF ABBREVIATIONS

D = dentine.
P = pulp tissue.
O = odontoblasts.
FM = fibres of Mummery.

THE SO-CALLED INTERSCAPULAR GLAND AND TUMOURS ARISING THEREIN

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INTRODUCTORY

In June 1920 at the Sydney Hospital, Sir Herbert Maitland operated on a female child, aged eleven weeks, for cystic tumour of the neck. The fact that the growth was found at operation to consist of three types of cysts, one containing clear fluid, one containing yellow semi-fluid material and one containing blood, suggested to him that the growth was a tumour of the so-called "interscapular gland of Bonnot," and he asked me to work out the pathology of the condition. To do this it was essential to render myself familiar with the normal anatomical and histological features of the "interscapular gland," and with work already carried out in this field by other investigators. The results of my investigations, while mainly confirmatory of the findings of other workers, have led me to form some opinions which are not in strict accord with those hitherto published, and I have thought it worth while to record them in detail as they have largely determined my attitude in regard to the interpretation of the anatomical and histological pictures presented by cystic hygromata and other allied tumours occurring in the neck and elsewhere.

HISTORICAL

Since the middle of last century opinions have varied as to the mode of development of adipose tissue in different regions of the animal body, as indicated by Batty Shaw (1902) (1) in his review of the literature on this subject. Many observers have insisted that in some situations such as the neck, axilla, mediastinum, subpleural and perirenal tissues, fat is stored in special cells set aside for that purpose, these cells being grouped together to form the so-called "fat glands" or "fat organs."

Other investigators have declared that there are no special fat glands but that all fat is deposited in fixed connective tissue cells and can be removed by starvation, the original simple form of the connective tissue cells being reproduced. The argument between these two rival schools of thought has largely hinged on the significance attached to certain cells which have been recognised by most workers in this field of study. These cells are large, rounded, or polygonal from mutual pressure, and have a finely granular cytoplasm.

Many of them are entirely free from fat, others however contain many small discrete globules of fat, giving the cell its mulberry or moruloid appearance. These moruloid cells tend eventually to assume the uniglobular form.

The material investigated by Batty Shaw was from the human subject. He recognised that in the human embryo subcutaneous adipose tissue contains fat deposited in connective tissue cells usually as a single globule, whereas adipose tissue in other sites such as the axilla and beneath the pleura shows the fat deposited in separate droplets to give the mulberry appearance. However he regarded the peculiar appearance of these fat cells, not as evidence favouring the existence of special fat glands, but merely as a metamorphosis occurring in the fat of the body reaching its maximum at, or before, birth in some quadrupeds, and in the infants he examined some two or three weeks after birth.

Hatai (1902)(2) published a paper on the presence in human embryos of an interscapular gland corresponding to the so-called hibernating gland of lower animals. In the adult subject he was unable to find any trace of a gland in a similar situation. Hatai describes the gland as a long narrow paired organ lying partly along the neck and partly occupying the scapular region. He states that the gland is composed of two entirely different constituent tissues, an outer fat tissue and an inner lymphoid structure. To be more precise the gland is composed of a large number of lymphatic nodules, each surrounded by a thick fibrous capsule, each or several of them being again surrounded by the fat tissue. The lymphatic nodules, he says, are composed of adenoid tissue which contains an abundant supply of blood and lymph sinuses and vessels. According to Hatai this peculiar organ corresponds to two organs of other mammals; one the so-called "hibernating gland" or fat organ, and the other the so-called "haemolymph gland." In this paper Hatai describes the topographical relations of the gland but omits a histological description.

Edmond Bonnot (1908)(3) investigated the problem in greater detail, studying not only the topographical relations of the gland but also its histology and histogenesis in man and various animals. He describes the exact limits of the gland which he regards as extending over a considerably larger area than did Hatai.

He speaks of the gland as a paired organ, very irregular in shape, but definite in outline, situated on the shoulder and side of the neck. In the adult cadaver the gland has a dark brown colour. In fresh subjects at autopsies the gland is pink in colour and lobulated, presenting much the appearance of fresh pancreas. In the new-born the gland is well developed and has a decided brown colour; the whole mass is lobulated, and these lobules are bound together by connective tissue septa. Were it not for the colour and definite outline of the gland it might easily be mistaken for fat.

Unlike Hatai, Bonnot found the gland to be present in the adult subject. Posterior to the internal jugular vein in the early embryo (11 mm.) are large irregularly scattered lymph sinuses. It is about these lymph spaces, Bonnot

states, that the gland is formed through proliferation of mesoblastic cells. The gland differentiates first into lobules having a structure different from any other in the body, second into lymphoid tissue, which further differentiates into haemolymph and lymph nodes. It is evident that the haemolymph nodes have to do with the formation of red and white blood cells. The large irregular cells in the lobules of the gland have the power of adjustment either to accumulate fat or to act as phagocytes for the broken down red blood cells. These large irregular cells in the lobules and similar ones in the gland nodes probably serve the same function.

Those in the lobules are evidently fixed cells, while those in the gland nodes may be wandering cells. The brown granules in the cells are blood pigment.

The interscapular gland is constant in all mammals and in man is probably the homologue of the so-called hibernating gland in rodents. That the structure functions under certain conditions as a storehouse for fat, as a scavenger for the red blood cells, and as a blood-forming organ, is rather hard to deny.

Shattock (1909)(4) published a paper on normal tumour-like formations of fat in man and the lower animals. Part of this work is devoted to the study of fat masses in the necks of Cretins. As a result of his studies Shattock formed the opinion that these fatty swellings in the necks of Cretins are not mere fortuituous local accumulations of fat, but that they are enlargements of structures similar to those found in the neck of the hedgehog. In a human foetus of about five months Shattock found that whilst the common subcutaneous fat showed the usual structure and consisted of unilocular cells of various sizes, that about the great vessels presented a markedly different aspect. His description of this deep fat is in accord with that of Bonnot. Shattock states that in the interscapular gland there is a variable number of lymph and haemolymph nodules which vary in different parts of the gland, but that in some of the gland processes such nodules are wanting. He does not hazard an opinion as to the function of these nodules or their relation, if any, to the glandular adipose tissue.

Shattock concludes that there are two forms of adipose tissue. One of these arises from a deposition of fat in common connective tissue cells, the fat, though deposited at first in droplets, eventually coalescing into a single sphere. The other is confined to particular areas, the fat being deposited in discrete droplets and remaining so, a form which histologically allies the cell groups to those of a ductless gland. The fact that in the hedgehog this gland-like adipose tissue in the neck does not, during hibernation, behave like the common subcutaneous fat (being reserved while the latter is undergoing absorption) indicates a physiological as well as a histological specialisation. Shattock realises the possibility of such fat being eventually replaced by adipose tissue of the common variety formed from the interlobular connective tissue by a process of fatty substitution of the kind witnessed in the case of the thymus.

Cramer (1920)(5) has studied glandular adipose tissue and its relation to other endocrine organs and to the vitamine problem. He suggests that glandular adipose tissue and the adrenal cortex have a similar function in reference to the metabolism of cholesterin and the other lipoids present in the adrenal cortex. His observations were made mainly on the perirenal fat of the rat and mouse. He states that, when examined in polarised light under crossed Nicol's prisms in frozen sections, many of the globules show very distinct double refraction. This anisotropic fatty material is mixed with isotropic fatty material; in other words, the globules contain a mixture of true fats and lipoids. Anisotropic material occurs not only in polygonal cells with a central nucleus and several globules but also in the large round cells with only one large globule, although in the latter there is a preponderance of isotropic true fat. When the relative amount of true isotropic fat increases, as it does in well nourished animals, the small granules as they increase in size tend to push the nucleus to one side of the cell and to coalesce into one large drop. In conditions such as fasting or restricted diet in which ordinary adipose tissue is greatly diminished the glandular adipose tissue persists and shows no obvious diminution.

PRESENT INVESTIGATION

My own study of glandular adipose tissue included material from a boy 16 years old and from seven foetuses, three full term, and one each at $7\frac{1}{2}$ months, 190 mm., 110 mm., 81 mm. (breech-vertex measurements).

I also had access to Professor Welsh's and Doctor Marjory Little's collection of early embryos cut in serial section through the thyroid region.

Macroscopically in fresh post-mortem specimens the differentiation of glandular fat from ordinary subcutaneous fat is easily made; the former is yellow, the latter a putty colour. There are, however, in the glandular fat many lobules which closely resemble ordinary adipose tissue, presumably because the fat cells are distended with isotropic fat as mentioned by Cramer. The vascularity of glandular adipose tissue is striking. It is much more vascular than ordinary adipose tissue.

In my investigations tissue was removed from the neck (superficial and deep) axilla, mediastinum, upper surface of the diaphragm, perirenal region, and groin.

Glandular fat was found in all the situations mentioned above the diaphragm. Speaking generally, below the diaphragm the characteristic histological picture was wanting, but in some cases perirenal fat and retroperitoneal fat around sympathetic ganglia showed characteristic cells with central nuclei and small fat globules. In the adipose tissue in the groins I did not detect any of these cells, all of the fat being present in connective tissue cells as large single droplets.

In studying the embryos I found that in the deep tissues of the neck the characteristic appearance of glandular fat could be seen before fat became

deposited in the subcutaneous connective tissue; and when fat first appeared in the subcutaneous tissue, the difference between the histological characters of this adipose tissue and those of the more deeply placed glandular fat was striking.

This is in agreement with the findings of Shattock and others that there are two types of adipose tissue which are histologically quite distinct. Hatai described the fat gland as a long narrow paired organ lying partly along the neck and partly occupying the scapular region. Bonnot described it as very irregular in shape but definite in outline, situated on the shoulder and side of the neck. My studies indicate that glandular fat is also present in the mediastinum and sometimes on the upper surface of the diaphragm. Some cells resembling those of glandular adipose tissue were seen in the perirenal fat and retroperitoneal fat, but speaking generally the adipose tissue in these situations contained large single fat droplets; still this may represent an exaggerated degree of the change seen in fig. 4, where glandular fat is, in places, losing its characteristic histological appearance as a result of fusion of small fat globules to form large single droplets.

The association between the lymph nodes and the haemo-lymph nodes on the one hand and glandular adipose tissue on the other hand was regarded by Hatai, and later by Bonnot, as sufficiently close to warrant them being regarded as separate elements of a composite single organ. I am inclined to think this an artificial union. I can see no more intimate relation between the lymph and haemo-lymph nodes in the neck or mediastinum with the adjacent glandular adipose tissue than there is between any lymph node and its surrounding adipose tissue, subcutaneous or deep.

Figs. 1, 2 and 3 are from the same normal foetus at full term.

Fig. 1 shows normal skin and subcutaneous adipose tissue. The large single fat spaces are conspicuous in the adipose tissue.

Fig. 2 shows glandular adipose tissue deep in the neck. The striking difference from ordinary adipose tissue is apparent. It is much more solid looking tissue than ordinary subcutaneous adipose tissue. Portion of a lymph node is shown in the bottom left-hand corner.

Fig. 3 reveals a lobule of glandular fat more highly magnified; the cells resemble those of the adrenal cortex; many of them are rich in protein, have central nuclei and a few small droplets of fat. In some of the cells the droplets have fused to form large droplets which push the nuclei to the sides of the cells.

Fig. 4 represents deep adipose tissue in the neck of a boy 16 years old. Below is a large area of typical glandular fat, above and to the left a lobule of ordinary fat, above and to the right a lobule of glandular fat in which many cells have been distended by isotropic fat so that they are indistinguishable from ordinary subcutaneous fat cells.

CASE I

History. G. S. (S.H. 404), a female, aged 6 weeks, was admitted to Sydney Hospital on 29 June, 1920. She had a cystic tumour on the right side of the neck (see fig. 5). At birth the swelling was the size of an orange. It steadily grew larger, extending towards the anterior aspect of the neck and pushing up the ear. At first it was quite soft (causing no obstruction to labour) but it became tender and more tense during the few days prior to admission.

Physical examination. Revealed on the right side of the neck a bilobed swelling the size of a foetal head. The lower swelling, just above the scapula, was soft and easily compressed, becoming tense when the infant cried. The

Fig. 5. The tumour before operation.

upper swelling extended to the border of the mandible anteriorly but did not involve the bone. Just below the ear, which was displaced upwards, was a soft cystic area that became tense when the infant cried. The posterior portion of the tumour was hard, brawny, red and hot, and the capillaries in the overlying skin were dilated. The tumour was irregular in outline and in consistence.

At operation. The upper part of the tumour was found to be a lymphatic cyst, the lower part to consist of numerous blood cysts with fluid contents. No definite capsule could be defined. The entire tumour was excised and no connexion with the large blood vessels was found. The tumour was situated beneath the sterno-mastoid and the upper part of the trapezius muscles.

Pathology

Macroscopic Examination

The specimen was received in several pieces. It consists of a collection of cysts of different sizes. The contents of the cysts vary. There are three types of cysts; firstly those with thin walls and clear fluid contents; secondly those with thin or slightly thickened walls, some containing almost pure blood, others blood-stained fluid in which is fibrin clot; and thirdly those with thick canary yellow semi-fluid contents and thick walls with ragged linings, the inner parts of the walls containing yellow material somewhat like the contents. The lining of the first two varieties is quite smooth, but there are complete and incomplete septa dividing the cysts into loculi. The skin over some of these lymph cysts and blood cysts is less than a quarter of an inch from the lumina of the cysts. Many of these cysts are quite small, even of microscopic dimensions. Of the cysts that contain yellow fluid the largest is about 1·5 cm. in diameter but the length is greater in some of them because the cavities are tubular. The walls of these cysts are, in some instances, 6 to 8 mm. thick; they are firm and apparently contain much fibrous tissue.

Microscopic Examination

Lymphatic cysts. The cysts containing clear fluid (lymphatic cysts) are lined by a single layer of endothelial cells and many of them are very complex. Complete and incomplete septa divide them into irregular compartments, and many strands or columns of connective tissue stretch from one wall to another. The congeries of cysts with associated fibrous tissue extends widely into adjacent structures and enmeshes portions of voluntary muscle, adipose tissue and nerves. Vessels form a conspicuous part of the tumour but it is difficult to determine whether any vessels are merely entangled in the fibrous overgrowth or whether they all form an essential part of the fibro-vascular neoplasm.

In size the lymphatic cysts vary greatly, from those which presented so conspicuous a feature in the gross specimen, to lymphatic spaces and channels showing little deviation from normal.

The lymphatic glands show all grades of involvement. In some the germ centres are conspicuous and there is catarrh and slight dilatation of the lymph sinuses as well as an increase in fibrous tissue patchy or diffuse.

The appearances presented by these glands might all be due to inflammation which is certainly responsible for conspicuous changes in some portions of the tumour, but I think it is difficult to exclude the possibility of this fibrosis representing a late stage in the evolution of the malformation. In other lymph glands (see fig. 6) the changes somewhat obscure the original structure. In this figure we see four altered lymphoid areas, increased fibrosis of the connective tissue stroma and a dilated lymph sinus. The structure of the tissue

adjacent to the portion illustrated shows that we are here dealing with changes in a lymph gland.

It is sometimes very difficult to tell whether a collection of cysts with small accumulations of lymphocytes in the septa has developed in a lymph gland or not. In fig. 7 is depicted a collection of cysts with one small dark area near the centre. This dark oval area represents a collection of lymphocytes, possibly a lymphoid area in a malformed lymph gland. The structure of the tissue adjacent to this field suggests that this is the correct interpretation. It is possible, however, that these cysts have developed in lymphatic vessels apart from lymph glands. This possibility should be kept in mind because in angiomata, both of blood vessels and of lymph vessels, situated at a distance from the normal sites of lymph glands, I have often noticed small collections of lymphocytes in the stroma. These lymphocytic accumulations may be merely inflammatory and incidental, but at times I have wondered whether they may not be an essential part of the lesion. When a lymph gland shows little lymphoid tissue and many spaces it does not necessarily follow that a lymph gland once normal has been transformed into a collection of cysts; on the contrary it seems likely that some of these cystic glands were never properly developed and that this abnormality constitutes part of the malformation.

The contents of the lymphatic spaces is mainly amorphous material which stains pink with eosin. It is to be seen at the top of fig. 8. Many of the cysts, however, contain much coagulated fibrin and partial organisation of these fibrin clots is a conspicuous feature in the sections. In many of the fibrin clots calcium salts have been deposited. The characters of the granulation tissue in an organising fibrin thrombus are seen in fig. 8. There are no features of special significance except the giant cells which show up as dark black areas. These giant cells apparently are helping to absorb the fibrin and they resemble the giant cells in the organising thrombi of thrombo-angiitis obliterans as illustrated by Buerger (6). I suspect on other grounds that so-called thrombo-angiitis obliterans may sometimes be associated with a congenital structural malformation of the affected vessels, and suggest that in that disease as in this case of congenital vascular malformation in the neck, the giant cells and the granulation tissue present no features of special significance.

Blood cysts. The second variety of cysts (blood cysts) varies considerably. Some of these cysts contain almost pure blood which in many is thrombosed and in some is partly organised. The characters of these thrombi are akin to those of the fibrin thrombi present in the lymphatic cysts. Some of the blood cysts contain fluid blood, and there is little doubt that many of these are lymphatic cysts into which haemorrhage has occurred. There is no conclusive evidence in this particular specimen that the blood cysts have not all formed in this way, for as Bland-Sutton (7) and others have pointed out, the walls of the lymphatic cysts in cystic hygromata of the neck are very vascular, and extravasation of blood into the lumina of these cysts is quite common. Nevertheless, I am of the opinion that many of the blood cysts in this specimen

were at the outset blood cysts and not lymphatic cysts. It has been my experience that angiomata in general often contain both blood vessels and lymphatic vessels. Sometimes the two are present in almost equal proportions, but usually either the lymphangiomatous or the haemangiomatous tendency predominates to such an extent that the growth assumes the clinical form of a lymphangioma or haemangioma. It is for this reason that I regard the conspicuous blood vessels in the walls of some lymphatic cysts as part of the growth and not merely the result of secondary inflammation.

The voluntary muscle in the vicinity of the cysts shows interesting changes (see fig. 9). Strands of connective tissue with conspicuous thick-walled vessels separate individual muscle fibres and groups of fibres one from another. The muscle fibres show considerable deviation from normal; some are larger, others smaller than normal. The large fibres have partly lost their affinity for the eosin and stain an orange colour. Many of the fibres that are cut longitudinally are seen to be irregular and wavy. This fibrosis may be the result of inflammation or may be an essential part of the malformation. While recognising that in those portions of the tumour where inflammatory changes are evident the fibrous tissue is probably scar tissue, I suspect that in some situations the fibrous tissue with its thick-walled vessels may represent a late stage in the malformation. In either case I suggest that it may be related to those curious examples of cicatricial contraction found in the necks of infants suffering from congenital torticollis and congenital elevation of the scapula.

Figs. 10 and 11 are taken from a vessel situated quite apart from lymph glands but in the vicinity of lymphatic cysts. The appearances in early sections of this vessel were so interesting that additional serial sections were cut. There is little doubt, I think, that the sections are very nearly at right angles to the long axis of the vessel. Fig. 10 shows a cross-section of the whole vessel which is quite isolated and not embedded in a dense mass of fibrous tissue. This isolation makes the increased thickness of the wall the more striking. The increase is mainly due to fibrous tissue in the outer coat; within this is a little involuntary muscle mingled with fibrous tissue and within this again is a layer of flattened endothelium. No internal elastic lamina is present so that the vessel is either a vein or a lymphatic. No red blood cells were seen in the lumina in any of the sections, and from its situation the vessel is most likely lymphatic. At the level depicted in fig. 10 there appear to be three lumina; in the right half of the figure thin processes project into the lowest lumen, and the septum between the lowest lumen and the right upper lumen seems almost angiomatous. At other levels these lumina are seen to communicate with one another. Some sections show two lumina, others only one. Fig. 11 shows the endothelial strands more highly magnified. The area illustrated in fig. 11 corresponds to the angiomatous septum in the right half of fig. 10, but it is taken from a section at a slightly different level.

After studying serial sections of this vessel I submit the following as a

tentative explanation of the sequence of events of which one phase is illustrated in fig. 11.

The endothelium lining the vessel proliferates to form a bud which elongates and is at first composed of two single layers of endothelial cells. At a later stage connective tissue is formed between these two layers of flattened endothelium, first appearing near the base of the endothelial process and later extending towards the apex. Endothelial lined spaces are formed in the connective tissue core in the process and also between plicated folds of thin portions of the process where these fuse laterally. The endothelial processes fuse not only with themselves, but also with adjacent endothelial processes and with the apparently normal endothelium lining the vessel. These endothelial bridges, when thickened and strengthened by connective tissue, form septa dividing the original lumen of the vessel into two or more compartments. The appearances depicted in fig. 11 resemble those of angiomata and not those of inflammation or repair. I have seen similar appearances in veins of the leg in a patient suffering from thrombo-angiitis obliterans, and this evidence I regard as an indication that at least in certain cases of thrombo-angiitis obliterans the vascular changes are due in part to a congenital malformation and are not purely of an inflammatory nature.

It is often stated that cystic tumours of the neck infiltrate voluntary muscle, but it seems more probable that the pathological process spreads by continuity along preformed channels and does not infiltrate in the sense that cancer or sarcoma does.

The malformation is not static; it may be progressive and the vessels may keep on "malforming," so that malformation and new growth are much akin.

The congenitally abnormal vascular tissue is predisposed to attacks of acute inflammation caused, not by a specific micro-organism, but by any suitable bacteria that may gain access to the susceptible tissue.

Cysts containing yellow fluid. An examination of the connective tissue beneath the skin and that between the cysts reveals a striking contrast between the structure of the adipose tissue immediately beneath the skin (see figs. 12 and 13) and the structure of the adipose tissue more deeply situated (figs. 14 and 15). Whereas the subcutaneous adipose tissue shows large round fat spaces with eccentric nuclei, the deep adipose tissue shows irregular fat droplets which are smaller and do not distend the cells. This is thought to be glandular fat which has departed somewhat from the characteristic appearance seen in a normal new born foetus.

The walls of the cysts with yellow fluid contents contain much fibrous tissue in which there is evidence of subacute inflammatory reaction, especially in the parts of the walls near the lumina. In addition to the inflammatory cells are others that closely resemble the cells of glandular fat (see figs. 16 and 18). Frozen sections of this tissue stained by Sudan III show that the spaces in the cells contained fat (see fig. 20). The contents of these cysts looked like pus but was largely altered fat and not true pus, though some pus cells and staphylo-

cocci were present. The cysts are thought to result from degenerative changes in glandular fat due to the strangling effects of the fibrous tissue which formed an important though relatively inconspicuous part of the tumour. The inflammation is a secondary phenomenon.

To speak of this specimen as a tumour of the interscapular gland is correct in that all three elements described by Bonnot are represented, but I think the same criticism applies to this specimen as to Bonnot's description of the normal gland, and instead of regarding this tumour as a composite growth, I consider it to be a haemangio-lymphangioma with secondary changes in the enmeshed glandular fat.

CASE II

History. W. J. (S.H. 4910), a labourer 31 years old, was admitted to the Sydney Hospital on 8 September, 1924, under the care of Doctor George Bell, to whom I am indebted for the clinical notes. The patient complained of a lump between the shoulders which was first noticed a year before admission and had gradually increased in size. He had been injured in this region during the war but no scar remained. The tumour had never been painful.

Physical examination. Revealed in the interscapular region and mostly to the left of the mid-line, a smooth lobular tumour about 10 cm. in diameter. The tumour did not appear to be attached to the overlying skin which contained numerous vessels that stood out distinctly, especially when the scapulae were drawn towards the mid-line.

Operation. On 10 September, 1924, under general anaesthesia, the tumour was removed by Doctor Bell. The skin in its vicinity was abnormally vascular. The tumour was composed of a deep orange-coloured tissue resembling fat, but more vascular than ordinary adipose tissue. In addition to the subcutaneous portion, a part of the tumour extended between the trapezius and rhomboid muscles on the left side. This portion also was removed. The patient made an uninterrupted recovery, and one year after the operation was in perfect health, and there was no recurrence of the growth.

Pathology

Macroscopic Examination

After twelve hours' fixation in Kaiserling's solution the tumour measures approximately 11 cm. × 8 cm. × 5·5 cm., but there are small outlying islets in the normal subcutaneous fat. The tumour is a putty colour, presenting a marked contrast with the canary-yellow subcutaneous fat and reddish-brown muscles. The tumour is lobulated, and between the lobules can be seen thin connective tissue septa. It resembles the interscapular gland fat in a normal foetus.

Microscopic Examination

Sections of the tumour reveal a structure closely resembling that of the interscapular gland of a human foetus at term. All grades of fat deposition may be seen in the cells of the growth. The characters of the cells are best seen in those portions where fat is inconspicuous. They are rounded, and each contains a small round nucleus with marked affinity for the basic stain. The nucleus is usually placed near the centre of the cell and is surrounded by granular cytoplasm in which fat droplets have been deposited. Where the fat droplets are moderately large and numerous they impart a mulberry

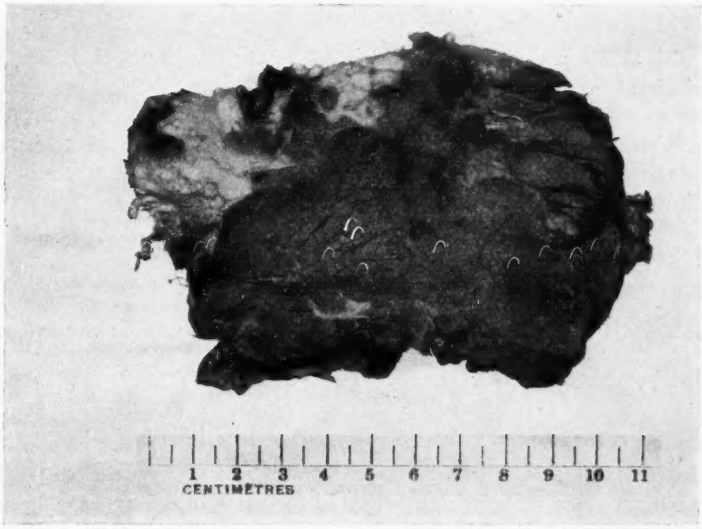


Fig. 21. A cross-section through the specimen removed at operation. Three structures may be recognised. The lower two-thirds of the specimen are composed of glandular adipose tissue. Above and to the left is pale subcutaneous adipose tissue. Above and to the right is a small portion of voluntary muscle.

appearance to the cell, and when the deposition of fat and the fusion of droplets is extreme the cell structure is completely obscured. Frozen sections stained with Sudan III showed the cells to be laden with fat.

It is possible that the tumour is an example of hypertrophy akin to that described by Shattock in Cretins, but on the whole I think the evidence suggests that the tumour is a true neoplasm, a "Lipoma Glandulare."

The vascularity of this growth has its counterpart in ordinary lipomata, for in them too vessels are occasionally so conspicuous that the tumours are angio-lipomata, and it is sometimes doubtful whether the stroma and its vessels are not more important than the fat-containing cells.

The only reference I have seen to a tumour apparently akin to this one is in a description of the Pathological Museum at the Annual Meeting of the British Medical Association held at Newcastle in 1921 (8). The specimen, which came from the West London Hospital, was referred to as a "lipoma glandulare," because the fat of which it was composed was arranged like that in the hibernating glands of animals.

All of the sections examined in this investigation were stained with haematoxylin and eosin with the exception of a few frozen sections that were stained for fat with Sudan III.

ACKNOWLEDGMENTS

I wish to acknowledge my indebtedness to the late Sir Herbert Maitland for bringing the first patient under my notice and for suggesting the diagnosis; to Professor J. T. Wilson for providing literature on the subject; to Professor D. A. Welsh and Doctor Marjory Little for giving me access to their serial sections through the necks of embryos; and to Doctor George Bell for supplying the clinical notes of the second patient.

SUMMARY

1. Part of the literature on "the Interscapular Gland" is briefly reviewed.

2. Histological examination of human adipose tissue, superficial and deep, before and after birth, gives support to the view that there are two varieties: (*a*) that composed of connective tissue cells, each distended with a single fat globule, such as is seen in subcutaneous adipose tissue, (*b*) that composed of rounded or polygonal cells with central nuclei and many small droplets of fat (mulberry cells) such as is seen deep in the neck, in the axilla, and in the mediastinum (glandular adipose tissue).

3. Glandular adipose tissue is found beyond the limits described by Bonnot for the interscapular gland. In particular it is found in the axilla, in the mediastinum and beneath the pleura.

4. Glandular adipose tissue is closely associated with lymph and haemolymph nodes, but no evidence was observed to support the view of Hatai and Bonnot that the association is so close as to warrant these structures being regarded as separate elements of a single composite organ.

5. Two tumours are described arising in the so-called "Interscapular Gland."

6. The first of these tumours, a congenital cystic tumour of the neck, consisted of three types of cysts, one containing clear fluid, one containing blood and one containing yellow semi-fluid material. This tumour is regarded as a haemangio-lymphangioma with secondary changes in the enmeshed glandular adipose tissue.

7. The lesion is a congenital malformation, but the malformation is not static. It appears to be progressive, the vessels continuing to "malform." Viewed in this light malformation and new growth are much alike.

8. Voluntary muscle adjacent to some cysts shows changes possibly akin to those occurring in congenital torticollis and congenital elevation of the scapula.

9. In some abnormal vessels angiomatous tissue extends from the walls into the lumina. Similar appearances have been observed in veins of the leg in a patient suffering from thrombo-angiitis obliterans. The opinion is expressed that in certain cases of thrombo-angiitis obliterans the vascular changes are due in part to a congenital malformation and are not purely of an inflammatory nature.

10. The second tumour, unlike the first, involved the glandular adipose tissue, not the lymph and haemolymph nodes. It is considered to be an example of "lipoma glandulare."

EXPLANATION OF PLATES I–VI

Fig. 1. Foetus, full term, showing normal subcutaneous adipose tissue (neck). ×60.
Fig. 2. Foetus, full term, showing normal glandular adipose tissue (neck). ×60.
Fig. 3. Foetus, full term, showing normal glandular adipose tissue (neck). ×250.
Fig. 4. Male, 16 years old, deep cervical adipose tissue showing transition stage. ×80.
Fig. 5. Text figure, p. 457.
Fig. 6. Portion of a lymph gland showing four altered lymphoid areas, increased fibrosis of the connective tissue stroma and dilatation of lymph sinuses.
Fig. 7. A collection of lymphatic cysts with complete and incomplete septa. The small dark area near the centre is a collection of lymphocytes, possibly a lymphoid area in a malformed lymph gland.
Fig. 8. Showing organisation of a fibrin clot in a lymphatic cyst. Above is faint amorphous material (the coagulated protein of lymph) which stains a faint pink colour with eosin. To the right are dense masses of fibrin (strongly eosinophilic). To the left is granulation tissue with dark staining giant cells near the centre of the figure. ×125.
Fig. 9. Thick-walled convoluted vessels in voluntary muscle with connective tissue passing between altered muscle cells, some of which are large, some small and some wavy. ×125.
Fig. 10. Shows a cross-section of a vessel thought to be lymphatic. At this level it has three lumina, at other levels two lumina or a single lumen. The septum between the lowest lumen and the right upper lumen seems almost angiomatous. ×65.
Fig. 11. Shows, under greater magnification, tissue corresponding to the angiomatous septum referred to in fig. 10. The plicated strand represents an early stage in the formation of a septum dividing up the original lumen of the vessel. The structure resembles that of angioma rather than that of inflammation or repair. Similar appearances have been observed in veins of the leg of a patient suffering from "thrombo-angiitis obliterans." ×250.
Fig. 12. Skin and subcutaneous tissue showing subcutaneous adipose tissue. ×30.
Fig. 13. The subcutaneous adipose tissue more highly magnified. ×250.
Fig. 14. Deep adipose tissue between lymphatic cysts. ×60.
Fig. 15. Deep adipose tissue more highly magnified. ×250.
Fig. 16. Inner part of wall of cyst containing yellow fluid. Inflammatory cells abundant. Below the centre are cells resembling glandular fat cells. ×125.
Fig. 17. Glandular fat cells under the same magnification from a normal foetus at term. ×125.
Fig. 18. Central portion of fig. 6 more highly magnified. ×250.
Fig. 19. Glandular fat cells under the same magnification from a normal foetus at term. ×250.

Fig. 20. Portion of tissue shown in fig. 8 stained with Sudan III to show the presence of fat in the glandular fat cells. × 250.

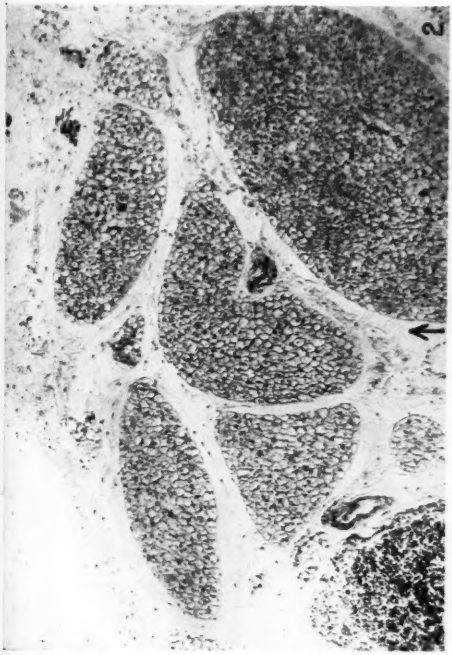
Fig. 21. Text figure, p. 463.

Fig. 22. Reveals the microscopic structure of the tumour in Case II. The resemblance to normal glandular adipose tissue is evident. The fat is deposited mainly in small droplets, but on the left of the figure a very large fat space is included. × 125.

The small arrow in each of the figures points towards the top of the figure as meant to be viewed in accordance with the descriptions in the text of the paper.

REFERENCES

(1) Shaw, Batty (1901–2). *Journ. of Anat. and Physiol.* vol. xxxvi, p. 1.
(2) Hatai, Shinkishi (1902). *Anatomischer Anzeiger*, Bd. 21, p. 369.
(3) Bonnot, Edmond (1908–9). *Journ. of Anat. and Physiol.* vol. xliii, p. 43.
(4) Shattock, S. G. (1908–9). *Proceedings of Royal Society of Medicine*, vol. ii, Part 3, Pathological section, p. 208.
(5) Cramer, W. (1920). *British Journ. of Experimental Pathology*, August.
(6) Buerger, Leo (1924). *The Circulatory Disturbances of the Extremities.* W. B. Saunders & Co. Chapters lxi and lxii.
(7) Sutton, Sir John Bland- (1922). *Tumours Innocent and Malignant.* Cassell & Co. 7th ed. p. 177.
(8) Annual Meeting Notes. *British Medical Journal*, Aug. 6, 1921, p. 213.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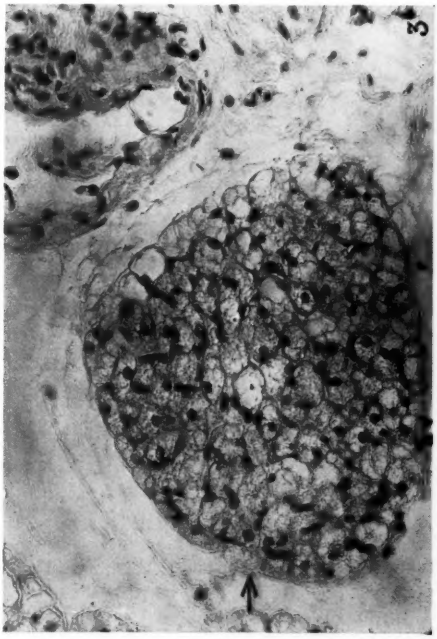
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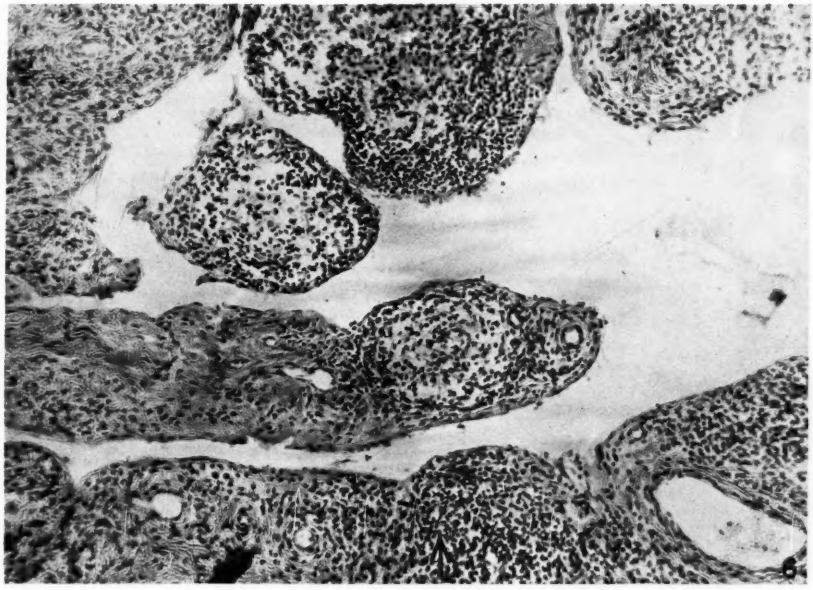

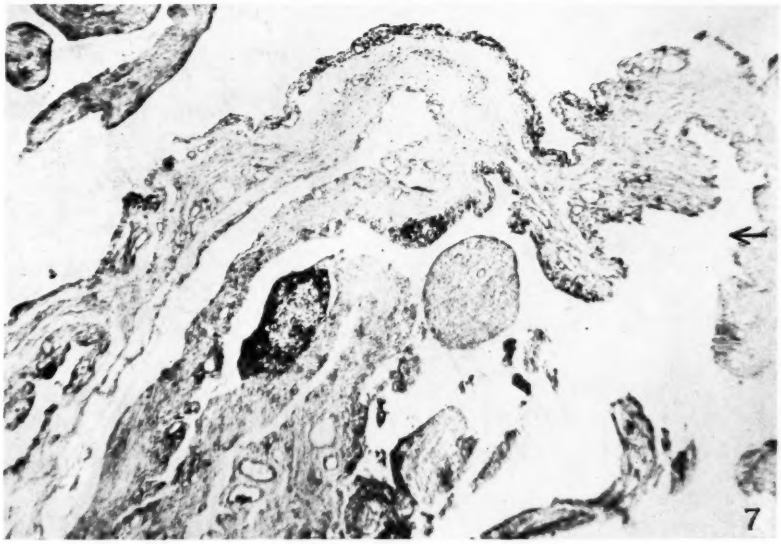

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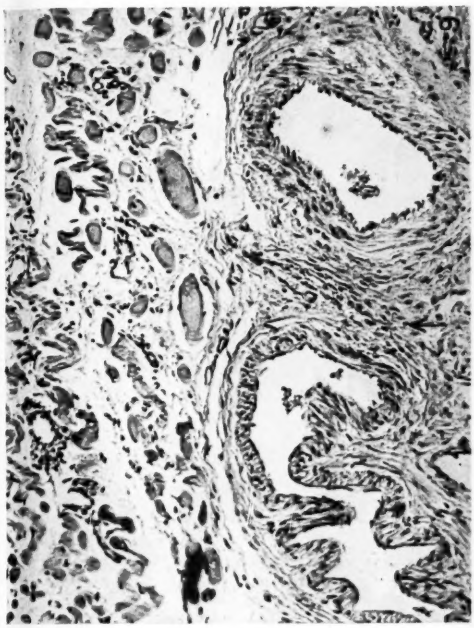

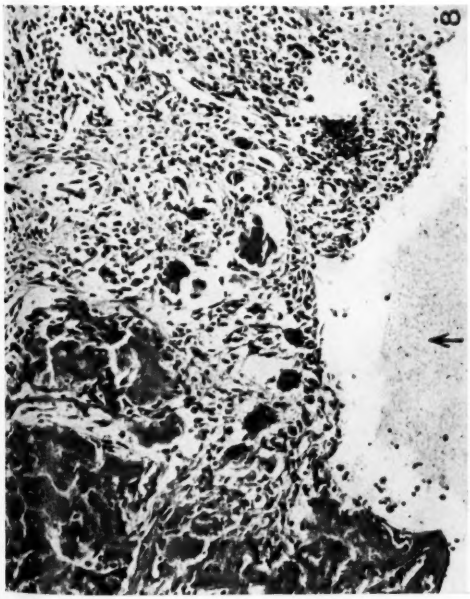

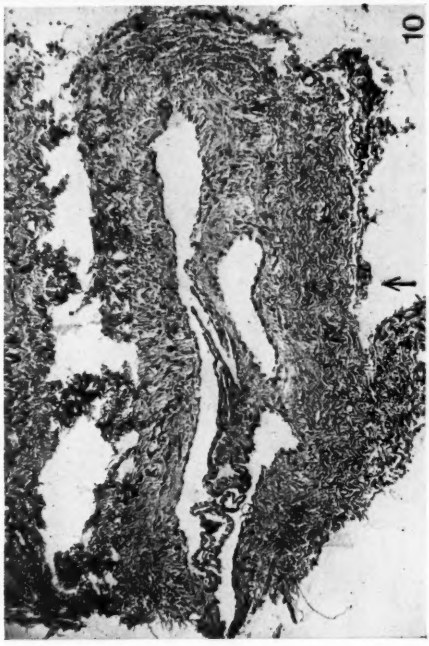

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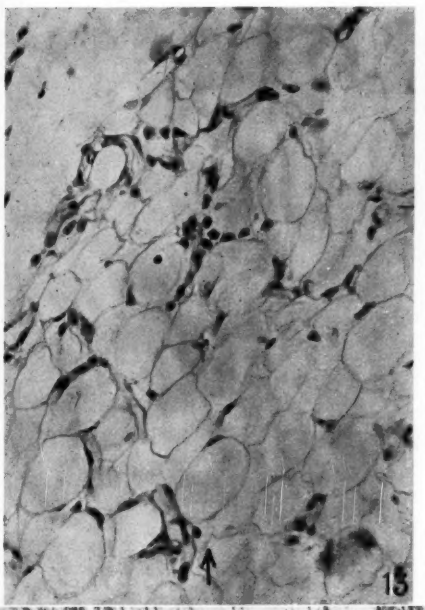
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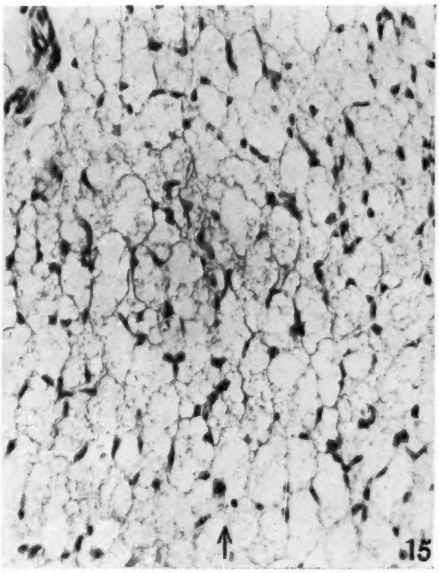
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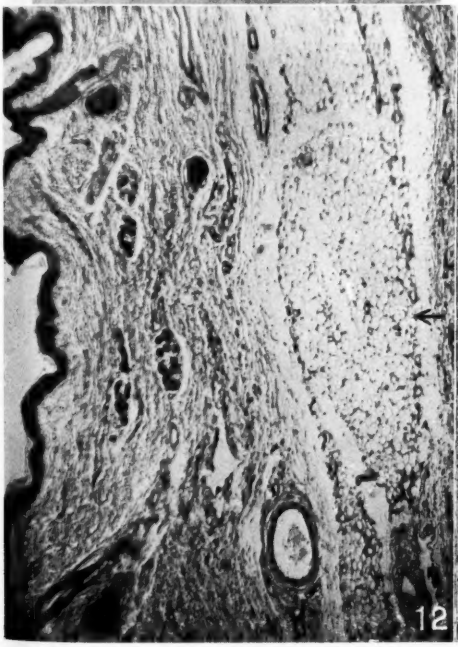
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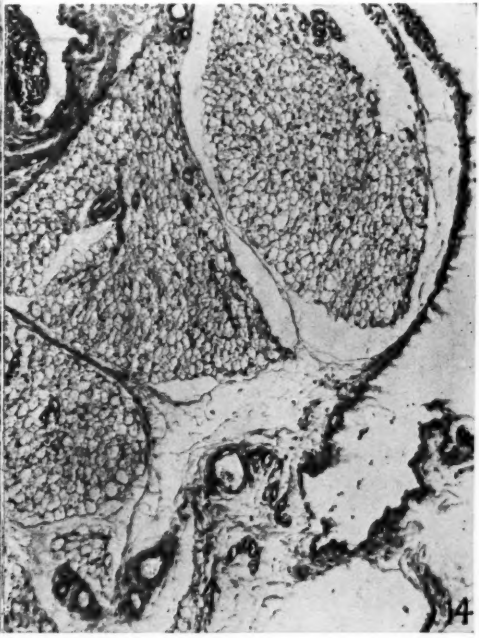
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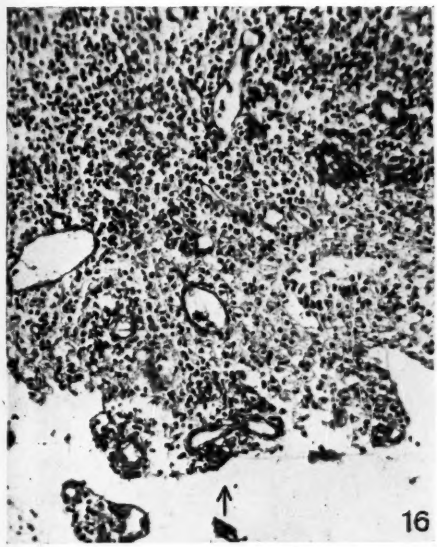
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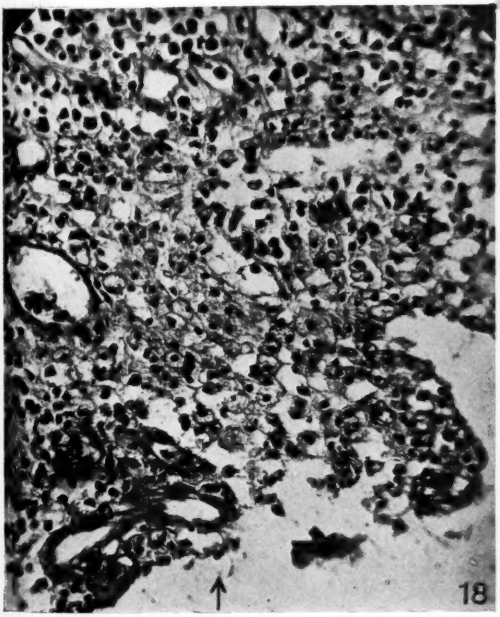
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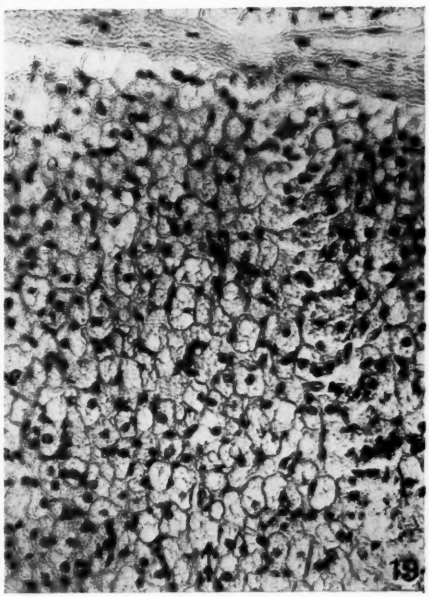
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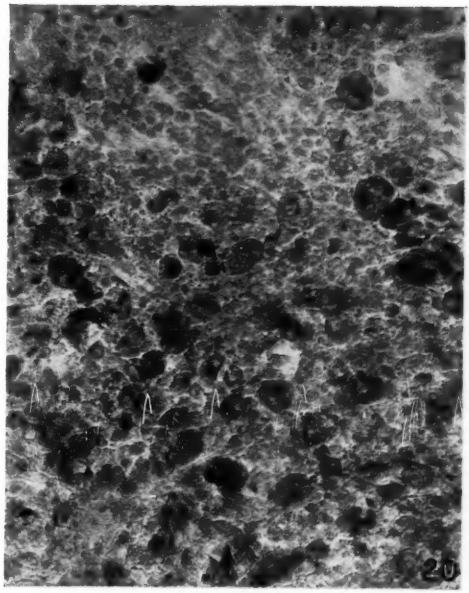
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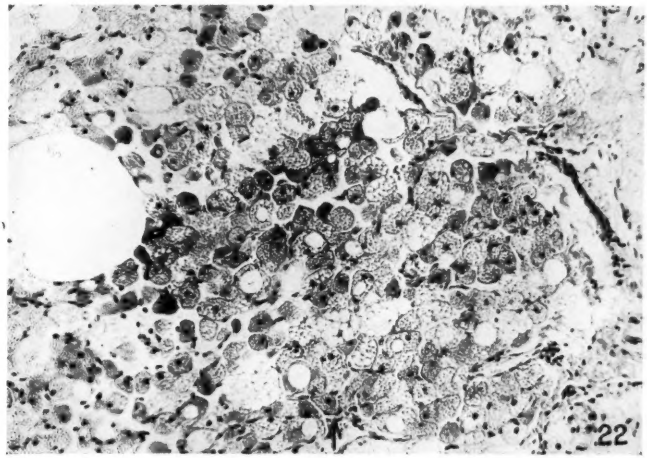
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DESCRIPTION OF THE CEREBRAL HEMISPHERES OF THE BRAIN OF A GORILLA (JOHN DANIELS II)

By W. E. LE GROS CLARK

In his description of anthropoid brains in the Catalogue of the Physiological Series of Comparative Anatomy in the Museum of the Royal College of Surgeons, Elliot Smith remarks in a footnote on p. 440 that "it is the apparently fortuitous variations in the Anthropoid Apes which point the way to the possibility of human evolution." For this reason, it appears desirable to place on record a brief description of a gorilla's brain which has lately come into the possession of the writer, for, although the literature dealing with the brain of this anthropoid is not scanty, the number of specimens of which descriptions have been recorded are relatively few.

The gorilla John Daniels II was the property of Miss Alyse Cunningham, to whom I am indebted for some interesting details regarding his habits during life. He was thought to be about five years of age and his weight in December, 1925, when he was in good health, was 110 lbs. He was evidently right-handed, though sometimes when told to shake hands, did so with his left hand. He died on 6 May, 1926, and a post-mortem examination indicated that ulcerative colitis was the cause of death. Immediately on death, the body of the animal was injected by Dr Vevers, of the Zoological Society of London, with a solution of formalin.

Before removal of the brain, the roof of the skull was removed and a photograph taken from above of the dorsal aspect of the cerebrum covered by intact membranes.

GENERAL OBSERVATIONS

The brain, on removal from the cranial cavity and with the leptomeninges still intact, was found to weigh 494·3 grm. Viewed from above, it is oval in outline, the frontal poles being broadly rounded and the occipital poles bluntly pointed. There is a distinct orbital keel. If fig. 3 is submitted to a general scrutiny, it will be at once observed (as one cannot fail to see in a general examination of the brain itself) that the surface of the parietal lobe is richly convoluted and plentifully furrowed by small secondary sulci in contrast to the broad smooth gyri which are found in the frontal and occipital lobes. This pronounced elaboration of the parietal cortex, limited as it is so sharply in front and behind by the central and lunate sulci, is, apart from size, perhaps the most striking feature to be observed in the Gorilla's brain when it is compared with that of Man. It is further emphasised by comparing

sections through the parietal, frontal and occipital lobes which are shown in figs. 4 and 5.

CEREBRAL CORTEX

Lateral Surface

The lateral fissure. The Vallecula Sylvii is deep and the stem of the Sylvian fissure is formed on both sides by actual contact between the orbital and temporal opercula. The orbital and fronto-parietal opercula are also closely approximated on the surface of the brain. This conspicuous development of the opercular formations in connection with the insula is somewhat astonishing. Elliot Smith (1) states that usually in the Gorilla the superior and anterior limiting sulci of the insula are separated by an exposed gyrus, so that the cortex of the island of Reil is superficially continuous with the frontal lobe of the cerebrum. On the left side of this specimen a small triangular area of the insula is exposed to view on the surface. On the right side, however, the insula is entirely buried from the surface so that it is not visible from a lateral view.

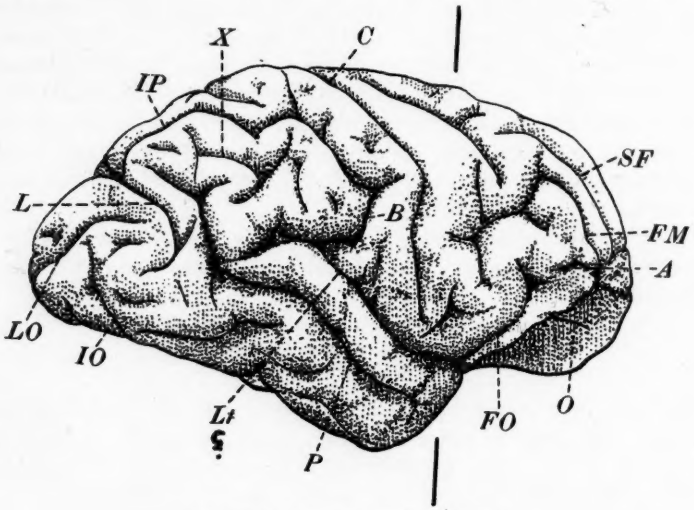

Fig. 1. Right cerebral hemisphere. ×¾.

The *insula* itself is also well developed. The superior border measures 37 mm., the anterior 22 mm., and the posterior 34 mm. All the limiting sulci are definitely opercular, especially the superior limiting sulcus. If the opercula are everted, it is seen that the superior does not actually join the anterior limiting sulcus, the *sulcus fronto-orbitalis*, but is separated by a small submerged gyrus. The fronto-orbital sulcus is continued up about half an inch

above the anterior extremity of the superior limiting sulcus. Each insula is bisected by a *sulcus centralis insulae*. On the right side, there are two main gyri breves in front and posteriorly one gyrus longus. On the left side, there are four gyri breves and a gyrus longus which shows an indication of a division into two parts. The main limb of the lateral fissure runs upwards and backwards and appears superficially to terminate on either side by a conspicuous bifurcation. The posterior limb of this fork is the real extremity of the Sylvian fissure as may readily be seen by slightly opening the lips of the sulcus. It is then seen that the anterior limb, which (again superficially) is continuous anteriorly with the lower end of the sulcus postcentralis inferior, ends just within the upper lip of the Sylvian fissure proper. The posterior extremity of the Sylvian fissure is depressed, running backwards with a slight downward

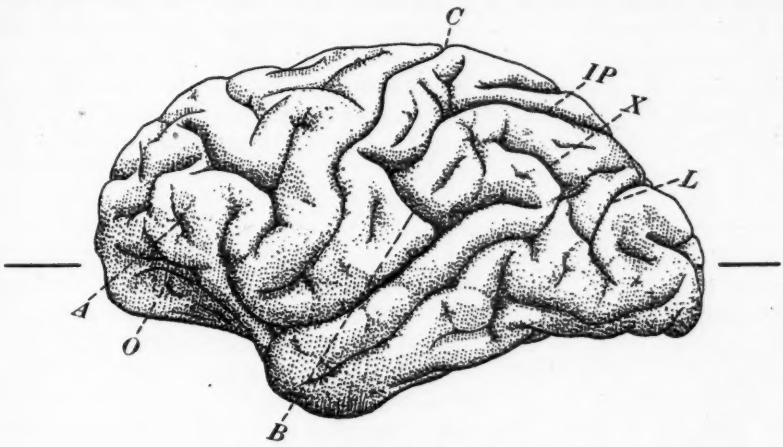

Fig. 2. Left cerebral hemisphere. $\times\frac{3}{4}$.

Figs. 1 and 2 are both drawn by means of a dioptograph. The planes of the sections figured in figs. 4 and 5 are indicated by lines.

tendency. This is in contrast with the condition in the human brain in which the caudal extremity usually curves somewhat sharply upwards. It may be noted that the posterior part of the Sylvian fissure in this brain is very deep.

The *sulcus centralis* runs an uninterrupted course downwards to terminate in the middle of the fronto-parietal operculum. On both sides, but rather more distinctly on the right, the upper end just cuts the dorso-medial border of the hemisphere. The genua of the sulcus are well marked on the left side, and a view of the dorsal aspect of the brain shows that on this side the whole of the sulcus has the appearance of having been thrust forward by the expansion of the parietal cortex. At a distance of 28 mm. from the upper end, the sulcus shows a forward convexity which lies in front of a sulcus projecting forward from the junction of inferior postcentral sulcus and the sulcus intra-

parietalis. A second forward convexity is situated at a point 54 mm. from the upper end, opposite the forward projection of the oblique sulcus, *B*, which appears to unite the Sylvian fissure with the inferior postcentral sulcus. At the upper end of this inferior convexity is a deep interlocking gyrus running from the precentral to the postcentral gyrus. The lower end of the left central fissure bears an intimate relation to the *sulcus subcentralis anterior*, but is separated from it by a slender exposed gyrus. On the right side, the central fissure is much straighter, but shows a curve corresponding to the inferior convexity described on the left side.

The Frontal Lobe

The *sulcus arcuatus* forms a conspicuous feature on either side, arching over the upper extremity of the fronto-orbital sulcus. On the left side, it is joined superficially at the junction of its vertical and horizontal limbs by the sulcus precentralis medius but separated by a submerged gyrus. On the right side, they are separated by an exposed gyrus. The horizontal limb of the arcuate sulcus bifurcates anteriorly, the dorsal branch appearing on the right side to join the posterior end of the *sulcus fronto-marginalis*. The latter sulcus pursues a course downwards and forwards towards the frontal pole of the cerebrum. In the somewhat broad cortical area lying between the anterior end of the sulcus arcuatus and the fronto-marginal sulcus above, and the orbital sulcus below, is a short oblique sulcus, *A*, which is better developed on the left side. The *superior precentral sulcus* runs downwards and forwards, its direction being much more oblique on the right side, so that the precentral gyrus broadens out considerably towards its centre. Just below the middle of the sulcus a branch is given off which is directed forwards on the left side, and almost directly medially on the right. This branch may be regarded as the posterior end of the superior frontal sulcus. The remainder of the *sulcus frontalis superior* is represented by three elements on the right side and two on the left. A *sulcus subcentralis anterior* is present on both sides. On the left, it is related very closely to the inferior extremity of the central fissure.

The Parieto-occipital Lobes

Sulcus lunatus. This very conspicuous fissure has a typical appearance. It is markedly opercular, and if the lips of the fissure are everted, its walls are found to be marked by small secondary sulci and gyri. The upper extremity of the sulcus just reaches the dorso-medial border of the hemisphere on either side. A section of the cortex in this region shows that the area striata extends to the free border of the opercular lip, where it terminates abruptly. On the lateral surface of the occipital lobe is a well-developed *sulcus occipitalis lateralis* which bifurcates posteriorly. On the right side, the upper limb of the Y so formed is detached from the rest of the sulcus. Immediately below the anterior end of this sulcus is a small secondary sulcus lying parallel with it, and below the centre of the lateral occipital sulcus is the upper extremity of

the large *sulcus occipitalis inferior* which runs downwards and forwards to reach the inferior border of the hemisphere. On the left side it becomes continuous (superficially) with the inferior temporal sulcus.

The *sulcus postcentralis superior* appears on both sides to join the inferior postcentral sulcus and the sulcus intraparietalis, but it is separated from both of these by a large submerged gyrus. The *sulcus postcentralis inferior* extends down as far as the level of the lower forward convexity of the central fissure where it appears to be joined by an oblique sulcus, *B*, to the lateral fissure as already described. In front of the inferior postcentral sulcus, the postcentral gyrus is marked by a short secondary vertical sulcus which, on the right side, is reduced to a mere dimple. The inferior extremity of the postcentral gyrus, in front of the oblique sulcus, *B*, is furrowed by another short vertical sulcus which again is better developed on the left side. This evidently represents the *sulcus subcentralis posterior*.

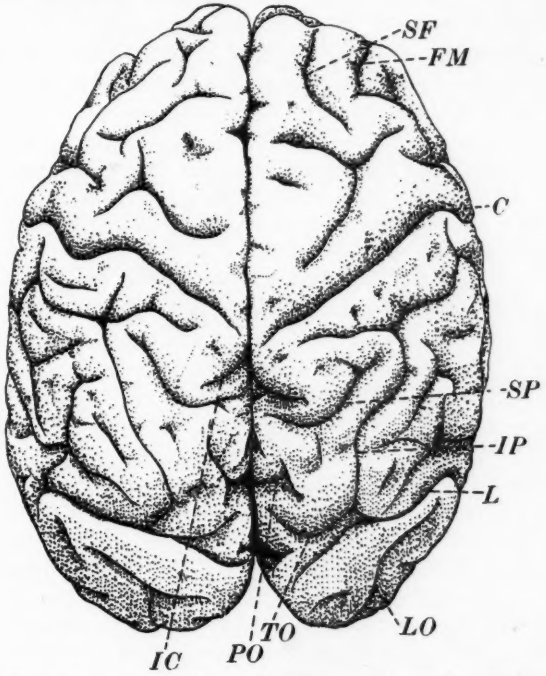

Fig. 3. Dorsal view of cerebral hemispheres. $\times \frac{3}{4}$. Traced with a dioptograph.

The *sulcus intraparietalis* joins (superficially) the inferior postcentral sulcus just above the centre of the latter. It runs an uninterrupted course, straight on the left but somewhat tortuous on the right side, to enter the lip of the lunate sulcus posteriorly. The *transverse occipital sulcus* on both sides is mostly

buried within the lips of the lunate sulcus except for its medial extremity which curls on to the surface and reaches the dorso-medial border of the brain. There is a well-developed *sulcus parietalis superior* which divides the superior parietal lobule into anterior and posterior moieties, both of which are indented by small secondary sulci. In front, the dorso-medial border of the brain is cut by the *incisura cinguli* which extends on to the lateral aspect of the brain for about half-an-inch. Behind is the *incisura parieto-occipitalis* forming here what is usually known as the external parieto-occipital fissure. Below the intraparietal sulcus the angular and supramarginal gyri are subdivided by conspicuous secondary sulci.

Temporal Lobe

The *parallel sulcus* is extensive. It begins anteriorly close to the tip of the temporal pole and pursues a straight course upwards and backwards. On the left side it curves round the posterior end of the lateral fissure and then runs upwards and forwards. This latter portion, however, is separated from the rest of the parallel sulcus by a submerged gyrus. On the right side this gyrus is widely exposed on the surface so that the terminal part of the parallel sulcus, *X*, is quite independent. The *inferior temporal sulcus* is broken up into three or four fragments.

The upper submerged surface of the superior temporal gyrus is furrowed by a series of shallow sulci which mark off three or four low rounded elevations anteriorly and a more distinct gyrus transversus posteriorly.

The Mesial and Inferior Surfaces

The *calcarine sulcus* forms an uninterrupted fissure, deeper in front than behind, and continued round the occipital pole on to the lateral aspect of the occipital lobe for about one centimetre. The formation of the *parieto-occipital sulcus* corresponds in detail to Elliot Smith's description of the essential composition of this complex. Thus there are three elements, the *incisura parieto-occipitalis*, a long fissure in front of this which runs downwards and forwards towards the precalcarine sulcus but is not in any way connected with it, and, behind, a short, relatively shallow fissure. A well-marked arcus curls round the inferior extremity of the incisura. Small sulci, apparently representing the sulci limitantes areae striatae superior and inferior, lie within the lips of the retrocalcarine sulcus. The *collateral fissure*, situated below and parallel with the calcarine fissure, is unbranched and extends forwards almost to the hippocampal fissure, its anterior extremity being separated by a short interval from the posterior end of the rhinal fissure.

The *occipito-temporal sulcus* consists of three elements, an anterior which is deep, extending back for 5 cm. from the inferior aspect of the temporal pole, and two small furrows posteriorly lying obliquely. On the right hemisphere, the most caudal element is connected superficially with the posterior end of the sulcus collateralis.

The *sulcus cinguli* commences below the genu of the corpus callosum and immediately behind the level of the upper extremity of the central fissure ascends vertically to cut the dorso-medial border of the brain. A short vertical branch is given off at about the level of the middle of the corpus callosum forming the anterior boundary of the paracentral lobule. This lobule is marked by a short *sulcus paracentralis*. The praecuneus is traversed by two short sulci, one of which continues on the direction of the sulcus cinguli, and the other runs upwards and represents a *sulcus praecunei*. There is a conspicuous *sulcus rostralis* in the usual position.

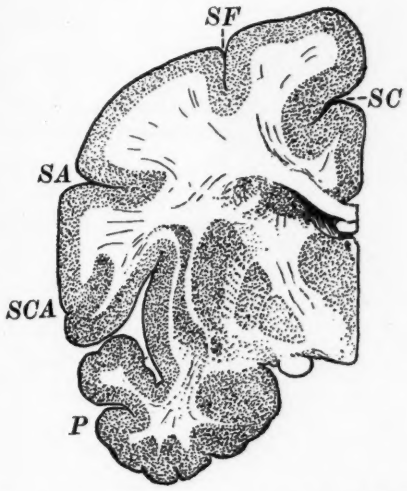

Fig. 4. Transverse section through the left cerebral hemisphere along the plane indicated in fig. 2. Nat. size.

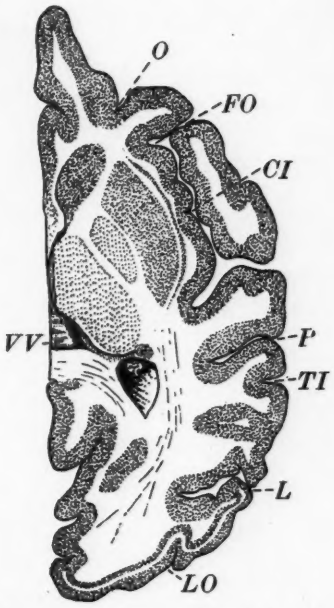

Fig. 5. Coronal section through the right cerebral hemisphere along the plane indicated in fig. 1. $\times\frac{3}{4}$.

The *rhinal fissure*, limiting the piriform lobe, is 22 mm. in length. The *sulcus orbitalis* on the right side forms a triradiate pattern. The main component runs parallel with the fronto-orbital sulcus and from its centre a branch runs forwards parallel to the olfactory sulcus. This triradiate sulcus separates off three areas each of which is indented in its centre by a small secondary sulcus. On the left side, the sulcus forms an H-shaped complex, the lateral extremity of the main component being terminated by a short transverse sulcus. The anterior area of the orbital surface on this side is crossed by a well-marked furrow which is an exaggeration of the small dimple to be seen in the corresponding position on the right side.

ASYMMETRY

After removal of the skull cap, a photograph of the dorsal aspect of the brain with membranes intact was taken in order to determine accurately what degree of general asymmetry there might be. As will be seen from fig. 6, there is certainly an asymmetrical condition posteriorly, in which the left occipital pole projects backwards rather more than the right. With this is associated a definite asymmetry of the superior longitudinal sinus, for, although this bifurcates at its posterior extremity, it divides unequally, the greater part

Fig. 6. Photograph of the dorsal aspect of the brain covered by membranes immediately after removal of the top of the skull, to illustrate the asymmetry of the hemispheres and the sagittal sinus. (Photograph by F. W. Bond, Esq.)

terminating in the right lateral sinus. The straight sinus was found to open in the midline at the confluens sinuum. An examination of the brain itself does not indicate any definite asymmetry in the fissuration of the occipital lobe except that the left sulcus occipitalis lateralis is more complete. Asymmetry is more to be remarked in the parietal lobes, for, on the left side, the cortical foldings show here a greater development than on the right. Such is indicated by the better development of the small secondary sulci, the pushing forward of the sulcus centralis and the more complete submergence of the

transverse occipital sulcus within the lips of the lunate sulcus. In connection with this asymmetry of the cerebrum, it may be noted that the evidence of the observers who watched the animal during life indicates that it showed a distinct preference for the use of the right hand in movements which required skill of any kind. I do not wish, however, to emphasise here a correlation between right-handedness and this type of asymmetry, especially that of the occipital lobe, for my own observations on the question seem to indicate that if there is any such correlation, it is very indirect.

SUMMARY

1. A brief description has been given of the cerebral hemispheres of a gorilla which had been kept under observation in captivity for a period of some years prior to death.

2. Attention has been especially drawn to the following points: the relative complexity of the parietal lobes in contrast with the frontal and occipital lobes; the remarkable extent to which the insula is concealed by surrounding opercula, so that the insula on the right side is completely buried from the surface, thus reproducing the condition to be found in the human brain; an asymmetry of the brain and venous sinuses which corresponds to the typical asymmetry of the human brain.

REFERENCES

(1) Elliot Smith, G. (1902). *Catalogue of the Museum of the Royal College of Surgeons of England*, vol. II, p. 439.

(2) Beddard, F. E. (1899). *Proc. Zool. Soc., London*, p. 65.

KEY TO TEXT-FIGURES

A.	See text	*O.*	*S. orbitalis*
B.	See text	*P.*	*S. temporalis superior*
C.	*S. centralis*	*PO.*	*S. parieto-occipitalis*
CI.	*S. centralis insulae*	*SA.*	*S. arcuatus*
FM.	*S. fronto-marginalis*	*SC.*	*S. cinguli*
FO.	*S. fronto-orbitalis*	*SCA.*	*S. subcentralis anterior*
IC.	*Incisura cinguli*	*SF.*	*S. frontalis superior*
IO.	*S. occipitalis inferior*	*SP.*	*S. parietalis superior*
IP.	*S. intraparietalis*	*TI.*	*S. temporalis inferior*
L.	*S. lunatus*	*TO.*	*S. occipitalis transversus*
Lt.	*S. lateralis*	*VV.*	*Ventricle of Verga*
LO.	*S. occipitalis lateralis*	*X.*	See text

ANATOMICAL NOTES

THE EAR OF CAROLAN, THE LAST OF THE IRISH BARDS

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An opportunity of examining the authentic skull of Carolan, the last of the Irish Bards (1670–1738), was recently afforded me by Professor Walmsley, and as it is current in anatomical literature that in musicians the inclination of the tympanic membrane differs from that in ordinary folk I examined the bony remains of the external ear with some care; and the findings are such that I think them worthy of record.

The external auditory meatuses are elliptical in sagittal section, the long axis being set, however, in the vertical and the short axis in the horizontal plane, and not as is usual oblique to them; at the isthmus of the canal the long axis is 8 mm. on each side and the short axis is 6 mm. on the right and 5 mm. on the left side. The canals pass inwards in a uniformly straight direction, that is, there is not, as is usual, a downward slope of the inner end of the tube beyond the isthmus; the length of the walls of the canals to the insertion of the tympanic membrane can therefore be easily measured. These measurements are as follows, and in brackets is the average measurement as given by Tröltsch:

	Right side	Left side
Anterior wall (16)	13 mm.	15 mm.
Posterior wall (15)	13 mm.	15 mm.
Roof (14)	14 mm.	16 mm.
Floor (18)	18 mm.	18 mm.

The left meatus is thus longer and narrower than the right.

The inclination of the tympanic membrane, as determined by a reconstruction of the meatus, was as follows: (1) To the vertical transverse (coronal) plane (fig. 1) the membrane sloped forwards and medially, and formed with

Fig. 1.

it an angle of 63° on the right side and 50° on the left side: this angle is not usually measured, but is stated to be about 55° (Symington). (2) To the horizontal plane (fig. 2) the membrane sloped downwards and medially and

Fig. 2.

formed with it an angle of 73° on the right and 76° on the left side; this angle, which is that usually measured as the angle of inclination, is given as 40° to 45° (Testut), a maximum of 54° (Forster)[1], and about 55° (Symington).

The tympanic membranes in this undoubtedly skilled musician[2] were, then, decidedly more vertical than is usual; and it is also recorded that the auditory meatuses had a straight course inwards.

[1] Forster, A., "L'inclinaison du tympan chez les mammifères supérieurs et chez l'homme," *Arch. d'Anat.* tome IV, 1925.

[2] Bardic music is remarkable for the use it makes of half tones and quarter tones in its cadences.

REVIEW

Anatomie Élémentaire des Centres Nerveux et du Sympathique chez l'Homme. By P. Gilis, Professor of Anatomy in the Faculty of Medicine of Montpellier. (Masson: Paris.) 1927. 20 francs. pp. 232. 35 diagrams and 1 plate.

The author has put together an elementary account of the cerebrospinal nervous system (the environmental or "vie de relation") and the autonomic nervous system ("vie végétative"). Two principles have guided him in his work. He emphasises the fact that there are not two independent nervous systems but that they stand in intimate physiological and anatomical relation to each other. Secondly, he wishes to bring out the enormous rôle now assigned to the autonomic nervous system, a rôle which makes it more extensive in distribution and function than the cerebrospinal system.

His information on the functional side has been obtained from French sources; on the anatomical side he has used Gaskell and Langley. The anatomical description calls for little comment. It is in accord for the most part with the teaching in this country. On the whole it is meagre, rather vague in regard to the innervation of blood vessels, alimentary canal, and ductless glands, and does not take account of more recent investigations. The illustrations are clear but some seem crudely schematic.

The importance of the autonomic nervous system in the author's eyes is best illustrated by the fact that it occupies as much space as the development and description of the cerebrospinal system. Everyone is familiar with the recent theories which make the autonomic system the basis of protopathic sensibility, postural tone, and even of all metabolic processes.

In general it would seem that these speculations have had some influence on the author. Though he refers to the metabolic activity of these nerves, and refers to such surgical practices as the Leriche operations, etc., there appears to be no reference to the double innervation of muscle. It is true that the author says that all the tissues of the body are innervated by the sympathetic nervous system.

An attempt is made to summarise the peripheral and central connections of the sympathetic afferents. The author accepts the position that there is no good reason to believe that these are other than cerebrospinal nerves which run in the sympathetic system. Since, as he says, the duality of the nervous system has only apparent justification at the periphery where the sympathetic elements are constructed on the preganglionic-postganglionic system, why call these fibres sympathetic? Gaskell's sympathetic nervous system was an entirely efferent one.

There is no index to the book.

Anatomical Society of Great Britain and Ireland

PROCEEDINGS

November, 1926 *February*, 1927
April, 1927

RECORDED BY
R. J. GLADSTONE

EDITED BY
E. BARCLAY-SMITH

PROCEEDINGS OF THE ANATOMICAL SOCIETY OF GREAT BRITAIN AND IRELAND

THE Annual Meeting of the Anatomical Society was held at the London School of Medicine for Women on Friday, November 19th, 1926, the President being in the chair.

(1) Professor WATERSTON showed lantern slides and portions of a skeleton from a short stone cist which he had investigated.

Apart from its antiquarian and anthropological features, the skeleton showed features of anatomical interest, such as evidence of inflammatory disease of some of the bones, extreme oblique wearing of the teeth, a large bony growth of the left hip bone, injury inflicted before death by a sharp weapon on the cervical vertebrae, penetrating the spinal canal, and blood staining which had persisted for between three and four thousand years of the upper part of the left humerus.

The PRESIDENT remarked that the appearance of blood staining of the upper part of the humerus in the specimen exhibited was very similar to the blood staining of bones seen in ancient skeletons in Egypt and Nubia. He considered that the osteophytic growths from the ischium were pathological, and that the changes in the bone resembled those of an inflamed surface.

Sir ARTHUR KEITH expressed a contrary opinion, saying that his impression was that the condition was not inflammatory. Marked changes are produced by the action of roots and water, on dead skulls found in cists, which might readily be mistaken for inflammatory changes produced during life.

Professor WRIGHT associated himself with Sir Arthur Keith with respect to the doubts he had expressed as to the inflammatory origin of the changes in the bones. He considered the specimen to be a typical example of the Aberdeen cist skeletons, and those of Taunton, E. Yorkshire, and the Isle of Wight.

Professor WATERSTON in reply said that he was familiar with the changes caused by weathering and erosion of dead bones, but that the constructive changes, and formation of local masses of bone, could hardly be explained as the result of weathering.

(2) Dr REAGAN with whom Dr MARGARET TRIBE was associated in the investigation read a paper on "The early development of the postrenal vena cava in the rabbit."

In anticipation of the failure to function, or of the derangement of the posterior cardinal veins, there is developed on each side, lateral to the aorta and also lateral to the periaortic sympathetic plexus, a plexus of capillaries (lateral aortic plexus). This extends from the mid-thoracic level practically to the sacral region. Its transverse elements drain the bases of the posterior cardinal intersegmental tributaries, and typically enter the transverse anastomoses between the posterior cardinal vein and the medial vessel of the mesonephros (subcardinal). In the course of development the longitudinal elements of the plexus become emphasised. In the caudal half of the thorax the longitudinal element, draining the posterior cardinal intersegmentals,

conveys its drainage caudally into the transverse element of the inferior vena cava (i.e. into the "renal collar" of Huntington and McClure). This thoraco-lumbar drainage on each side performs the function of draining the caudal thoracic intersegmental veins which are now abandoned by the disappearing posterior cardinal. Thus it is a functional substitute for the posterior cardinal vein pending the establishment of an azygos system. The thoraco-lumbar drainages apparently furnish no adult derivatives.

In the lumbar region, posterior to the potential transverse element of the postrenal vena cava, the longitudinal element of the lateral aortic plexus becomes closely applied to the bases of the more cranial posterior cardinal tributaries. The latter are so pressed toward the median plane by the migrating metanephros that very soon the observable remains of the plexus appear as if they were so many longitudinal fusions between adjacent intersegmental veins. But in the case of the second and third segments cranial to the future iliac anastomosis the kidney has migrated medially to the posterior cardinal intersegmentals, and has caused them to bow laterally. In these same segments the longitudinal element of the lateral aortic plexus drains the laterally bowed tributaries by means of transverse elements of the plexus. These soon develop into large structures and superficially resemble true posterior cardinal intersegmentals in general appearance. On each side, in the lumbar region, the longitudinal element forms a postrenal vena cava. The right persists. The first tributaries to the developing vena cava are the posterior cardinal intersegmental tributaries. The links between them consist of the transverse elements of the lateral aortic plexus. In the cranial region of the postrenal vena cava these linkages are soon lost sight of and the posterior cardinal intersegmentals appear to have direct entry. In the caudal region of the postrenal vena cava, exclusive of the last segment, the linkages retain their importance for a considerable time.

The transverse element of the postrenal vena cava (a portion of the renal collar) consists in part of the anastomosis between the posterior cardinal and mesial cardinal (subcardinal), and in part of a persistent transverse element of the lateral aortic plexus. The latter part corresponds to the subcardinal-supracardinal anastomosis of Hunitngton and McClure. But since the transverse elements of the lateral aortic plexus appear before a longitudinal vena caval line is formed, the derivative of the transverse element of the lateral aortic plexus cannot be said to be an anastomosis between the forerunner of the vena caval line and any other structure. Originally it is an anastomosis between the base of the posterior cardinal intersegmental and the anastomosis between the posterior cardinal and the mesial cardinal.

The thoraco-lumbar drainage does not lie medially with reference to the sympathetic trunk. It therefore does not lie in the line of azygos development. For a time it coexists in five or six thoracic segments with the azygos line. In previous accounts of development of the dorsal body-wall veins it has probably been confused with the forerunners of the azygos.

The plexiform forerunners of the main parts of the azygos and hemi-azygos line develop uninterruptedly in a caudal direction as far as the sacral region. They lie ventral and medial to the sympathetic trunks. They do not persist as continuous longitudinal structures in the adult. Azygos vein and postrenal vena cava are not a part of one uniform system of veins in linear continuity. The azygos line extends from the cranial cervical region to the sacrum. The venous line from which the vena cava develops is parallel to the azygos line

in the caudal half of the thorax and in the lumbar region and lies ventro-lateral to it.

The relatively simple hypothetical system of a single longitudinal venous line on each side for the functional replacement of the posterior cardinal vein is inadequate to explain the facts of development or the recorded anomalies in the foetus or adult.

Several of the facts herein recorded were first observed in the work of Robinson and Reagan, whose account accompanies this. Conversely, some of the facts first noted in our own work appear in the account by Robinson and Reagan. For purposes of record it has been agreed to confine this account to early development, and that of Robinson and Reagan to the later stages.

We desire to thank Professor J. P. Hill in whose laboratory our work is proceeding.

(3) Dr Reagan with whom Professor Robinson was associated in the investigation read a paper on "The later development of the inferior vena cava in man and in carnivora."

The derivatives of the *lateral aortic plexus* have been described in the foregoing account by Reagan and Tribe. The longitudinal thoracic elements of the plexus may be called thoraco-lumbar veins. The longitudinal elements in the lumbar region during their embryonic state of bilateral symmetry may be called para-ureteric veins. The left disappears. The right persists as the morphologically longitudinal part of the postrenal vena cava. The term "supracardinal" is not applicable to the structures which we have designated para-ureteric veins, since they are not serial homologues of azygos veins.

The longitudinal elements of the lateral aortic plexus receive the drainage of the adjacent posterior cardinal intersegmental veins for a considerable period of development subsequent to the degeneration of the posterior cardinals themselves.

Where a lateral aortic plexus exists (see Reagan and Tribe) its longitudinal elements are the first functional substitutes for the posterior cardinal vein.

The second functional substitute for the posterior cardinal vein develops as a longitudinal element (with transverse tributaries) out of a plexus which we propose to call the *perisympathetic plexus*. It may perhaps be comparable to the *periganglionic plexus* of Frazer though the identification of the two is very imperfect. At appropriate stages its transverse elements can be seen closely surrounding the sympathetic trunk at all levels, and not merely at ganglionic levels. In early stages it has a direct arterial supply from the bases of the dorsal aortic rami, and is drained into the bases of the posterior cardinal intersegmentals by vessels (basal anastomoses) both dorsal and ventral to the sympathetic trunk. The longitudinal element appears in the plexus as a capillary enlargement ventral and medial to the sympathetic trunk. In the cranial part of the thorax on each side, this longitudinal vessel which we designate as medial sympathetic vein (equivalent to the thoracic "supra-cardinal" of Huntington and McClure) develops strong direct connections with the posterior cardinal vessel. Whereas blood originally flowed from the perisympathetic plexus to the base of the posterior cardinal intersegmentals coursing through the *basal* anastomoses, the direction of blood becomes reversed. The medial sympathetic vessel increases in size, drains strongly into the posterior cardinal, and thus causes blood to flow from the posterior cardinal intersegmentals into the basal anastomoses. These drain into the longitudinal

element of the perisympathetic plexus. The basal anastomoses ventral to the sympathetic trunk soon degenerate. Those dorsal to it constitute the central portions of the typical azygos tributaries which pass dorsal and medial to the sympathetic trunk. In the cranial portion of the thorax (excluding from consideration the superior intercostals) the medial sympathetic veins are the only functional substitutes for the posterior cardinal.

In the caudal thoracic region the medial sympathetic is at first drained by transverse connections, into the thoraco-lumbar vein. The medial sympathetic or azygos line gains the ascendancy and comes to drain the thoraco-lumbar vein and its peripheral (posterior cardinal intersegmental) tributaries.

From the first time of their establishment throughout the lumbar region the medial sympathetic veins are strongly drained transversely, at intersegmental levels, into the ventro-laterally situated para-ureteric veins. These have as their original tributaries the peripheral intersegmental tributaries of the posterior cardinal which have been transferred to them. Temporarily the para-ureteric vein drains the posterior cardinal tributaries and also drains the medial sympathetic vein. The latter in turn has its own, at first feebly developed, intersegmental tributaries (dorsal basal anastomoses), which peripherally also drain the original posterior cardinal intersegmental veins. The latter then have two drainages into para-ureteric, an older direct one which lies entirely lateral to the periaortic sympathetic plexus, and a newer indirect one which passes dorso-medial to the sympathetic trunk, and enters the medial sympathetic which in turn drains into the para-ureteric vein; the older of these drainages disappears, and the newer more medial one persists, as the longitudinally directed medial sympathetic vein, until the (human) embryo is about 40 mm. long. The conditions described apply to either side of the body. The dorsal basal anastomoses are characterised by the fact that they lie ventro-lateral to the dorsal aortic rami, and pass dorso-medial to the sympathetic trunk.

Practically coincident with the development of, and in intimate relationship with, the perisympathetic plexus there appears dorsal to the aorta and medial to the dorsal aortic rami a diffuse capillary plexus (dorsal aortic plexus of L. H. Strong, 1926). On either side in the caudal thoracic and lumbar regions, just medial to the bases of the dorsal rami, there appear within the plexus longitudinal vessels provided with fine tributaries which course dorso-medial to the dorsal aortic rami. These veins (subcentral veins) tend to fuse into a single vessel, especially in the lumbar region. In some animals varying portions of the adult azygos lines are seen to lie dorso-medial to the dorsal aortic rami. Such portions of the azygos lines are derivatives of the subcentral vein or veins.

In man the lumbar subcentral vein becomes of great prominence. It has conspicuous transverse connections with the lumbar medial sympathetic veins, especially at intersegmental levels. At about the 42 mm. stage in the lumbar region of man its tributaries functionally replace the direct tributaries to the medial sympathetic veins (dorsal basals). Intersegmental drainage passes from peripheral remains of the posterior cardinal intersegmentals directly into the subcentral vein. This drains into the medial sympathetic veins. Of the latter the right one is becoming the larger; the left one shows signs of degeneration owing to the degeneration of left para-ureteric. By the time the foetus is 66 mm., the left medial sympathetic vein has entirely disappeared. The right medial sympathetic vein has ceased to exist as a longitudinal vessel, but

persists intermittently to form the base of the Y-shaped drainage of the lumbar veins into the definitive postrenal vena cava. Also the subcentral vein has degenerated except at points where it represents the region of meeting of the lumbar veins to form a single vessel.

It will be remembered that the most caudal pair of lumbar veins enter the vena cava separately. The right vessel of this pair has relationships with the sympathetic trunk reminiscent of the posterior cardinal intersegmental system.

The great development of the postrenal vena cava and the lateral displacement of the right sympathetic trunk cause the vena cava to lie in the concavity of curvature of the peri-aortic sympathetic plexus.

In carnivora the ventral displacement of the dorsal aorta, the close approximation of the sympathetic trunks, the degenerate condition of medial sympathetic and subcentral veins, and the dorso-medial location of the para-ureteric veins give the para-ureteric lines the superficial appearance of being azygos homologues.

A portion of this work accomplished by the junior author prior to a programme of collaboration is now in the press. For the courtesy of his laboratory and much technical assistance by his staff we beg to thank Professor J. P. Hill.

Professor Wilson referred to the hydraulic forces exerted in a growing organism, as producing changes in blood pressure, which would determine the course of blood through one or other channel of a capillary plexus; and gave as an example the opening up of blood channels in the vascular area of the chick.

(4) Mr E. Yule contributed a paper on "The arterial supply of the duodenum" which will be published in full, in the *Journal of Anatomy*. He showed that in addition to the ventral branches of the superior and inferior pancreatico-duodenal arteries each of these vessels gives off a dorsal branch, and that these branches anastomose on the deep aspect of the head of the pancreas. He considered that the continuity in the anastomosis of both the ventral and dorsal branches of these vessels precluded any deduction being made as to a limit in the adult duodenum between that part which is developed from the foregut, and that part derived from the midgut.

Professor Frazer said that, in the third month foetus, there was a connexion between the arterial supply of the mesoduodenum from the coeliac axis and neighbouring branches of the superior mesenteric artery. He considered that the anastomosis with the superior mesenteric artery was probably a secondary condition, and did not represent the early embryonic supply.

(5) Professor F. G. Parsons and Mr D. A. Davies submitted a paper on the "Radiographic study of human epiphyses." The age and order in which the epiphyses appear were considered. This will be published in the *Journal of Anatomy*.

Professor Elliot Smith remarked on the wide range of variation in the date of appearance of ossific centres. With reference to the union of the two segments of the ischiopubic ramus he drew attention to the importance of the view, as taken with the X-rays, being perpendicular to the plane of the pubic ramus, as otherwise a union might appear to have taken place, which had not yet occurred.

In an anencephalic foetus ossification of the epiphyses took place earlier than usual.

Union of the epiphyses was as a rule earlier in the female than in the male.

Professor STOPFORD mentioned a case of exophthalmic goitre, in a girl aged 12, in whom the secondary sexual characters had developed early. All the epiphyses were united, with the exception of the upper ends of the fibulae.

Professor PARSONS, referring to the union of the ischiopubic rami, said that there was no doubt of the union having taken place in the cases examined. He considered that the erratic variations in the ossific centre for the lower end of the fibula might be explained by variations in the size of the cartilaginous mass. If large, the centre was deposited early. The degree of vascularity of the part also had an important bearing upon the ossification of the epiphysis.

Professor ELLIOT SMITH referred to pathological causes of delay in the union of epiphyses, and cited the Pharaoh, Tutankhamen, who was believed to have been affected by Dystrophia adiposa genitalis, which may have caused a delay in the union. This may account for the discrepancy in his age 20–25, as estimated by Anatomists, and the historical age given as 30.

(6) Dr G. P. WRIGHT read a paper on "Some factors in tissue-culture."

In 1912 Carrel and Burrows discovered that the tissue extracts made from chick embryos exercised a great growth stimulating action on cells grown in tissue cultures. It remained obscure whether the substances in the extract which were responsible for this were formed in the embryo during the course of development or whether they were generated in the yolk sac and merely circulated in its body fluids, having been carried there by transportation in the yolk sac circulation.

Experiments were carried out to see if the yolk contents of the yolk sac had any growth stimulating action when they were added directly to tissue cultures. It was found that no such stimulation occurred. It had however been observed previously that the substances responsible for promoting growth were capable of passing through a collodion dialysing membrane quite impermeable to the proteins and fat droplets of the yolk. Since Carrel and Baker had associated lipoids with growth inhibition it was decided to attempt the dialysis of the egg yolk in a manner similar to that of the embryo extract.

This was carried out on both fertile eggs which had undergone no incubation and on those which had been incubated for seven days. In both cases controls were set up in saline and the average number of mitotic figures present in a series of cultures was used to determine the presence or absence of the growth stimulant. The following were the results:

	Medium used	
	Saline	Yolk diffusate
Fertile unincubated egg: Average number of mitoses	71	19
Fertile egg incubated 7 days: Average number of mitoses	14	127
" " " "	14	114

It appears therefore that in the incubation of the egg certain substances are produced in the yolk sac which greatly stimulate mitosis in embryo heart cells. Such substances are water-soluble and readily diffusible and appear to be separable from the proteins and fats of the yolk. In these particulars the growth-promoting substances resemble the water-soluble vitamins.

Dr REAGAN drew attention to the desirability of drawing a distinction between the kind of yolk employed in tissue culture, namely, white-yolk, or

yellow-yolk. The subgerminal fluid has a stimulating action on growth. A differentiation should be made between the two types.

(7) Mr H. A. Harris read a paper on "The growth of the long bones in childhood with special reference to bony striations of the metaphysis and to the rôle of the vitamins."

Certain transverse striations of the long bones are described in non-rachitic children who have suffered from various acute illnesses. The growth of the long bones have been traced radiographically in a child who suffered from successive attacks of broncho-pneumonia over a period of two years. All growth in length takes place at the growth cartilages and there is no interstitial growth in the shaft. Thus the "lead-shot" experiment of John Hunter stands confirmed.

Transverse striations are shown to be manifestations of cessation of growth. They occur normally in the first week of life and in adolescence; they may occur with seasonal variations in the rate of growth; they occur in all cases of marked decrease in the rate of growth as a result of any form of acute illness or starvation. They also occur as part of the healing process of rickets.

The skeletal processes are analysed in terms of (1) the area of cartilage proliferation, (2) degeneration and calcification of the cartilage, and (3) ossification proper. These areas are related to (1) a water-soluble growth-promoting vitamin or vitamins, (2) the enzyme of Robison or vitamin D, and (3) the fat-soluble vitamin A proper. These processes were discussed in terms of the archusia or growth-promoting principle, and the ergusia or differentiating principle of Burrows, as enunciated for results obtained from cultures of normal and pathologic tissues. A rational basis is adduced for the analysis of the processes involved in diseases of bone, applicable to all ages.

The interpretations of the various "schools" concerning the agents and methods of healing rickets are considered, and the fallacies of the "line test" were indicated.

The term "growth-promoting" as applied to vitamin A is a misnomer. The growth-promoting vitamins are water-soluble.

FEBRUARY, 1927

An ordinary meeting of the Society was held at St Mary's Hospital Medical School on Friday, February 4th, the President, Professor Elliot Smith, being in the Chair.

(1) Dr A. J. E. Cave read a paper on "Bilateral and unilateral thinning of the parietal bone."

Bilateral, or symmetrical, thinning of the parietal bone occurs macroscopically in one of two forms, either as (*a*) an area of flattening, triangular or quadrilateral in shape, or as (*b*) a broad sulcus, groove, or hollow, antero-posterior in direction, in the hinder part of the affected bone. (The case exhibited, the calvarium from an adult male over 40, belonged to the second type.) In neither form, however, is there any inward bulging of the calvarium at the site of the anomaly, where the bone is translucent and abnormally thin. Microscopically the pericranium and dura are normal, the compact tissue of the tables is somewhat more stratified than usual, and the diploë is absent, allowing the two tables, each normal in itself, to approximate. This absence of the diploë is the characteristic feature of the condition, which is essentially a growth-defect or dysplasia of the parietal diploë, resulting in approximation

of the inner and outer tables and a translucency of the bone consequent upon the thinness of the affected region in comparison with surrounding areas of normal bony thickness. The condition is not confined to the parietal, but may affect the frontal bone or the supra-inial portion of the occipital: it is congenital inasmuch as it is not an acquired defect, although not manifesting itself in infancy because then, normally, the diploë has not yet appeared. It affects both sexes impartially and has been observed in Europeans and also in Ancient Egyptian peoples. Its exact frequency is difficult to determine, but it is probably a much commoner condition than is usually believed.

Virchow, Rokitansky, Paget and others held the condition to be in the nature of a senile atrophy; Carriere and Gall, an excessive physiological atrophy; Jonathan Hutchinson thought syphilis a factor in its causation, Humphry, a stretching of the occipito-frontalis tendon, whilst Professor Elliot Smith has declared (and still maintains) it to be due to the wearing of heavy wigs (pressure atrophy). Recently D. M. Greig (*Ed. Med. Journ.* Nov. 1926) has admirably summarised our knowledge of this anomaly, and pointed out its true nature. Unilateral parietal thinness, of the same nature as the symmetrical condition, is unknown, save for a very dubious case of Bergmann's, insufficiently reported by Bloch (*Prague Med. Woch.* 1897). The specimen now exhibited, the calvarium of a male aged 47 having a single, inch-long depression in the right parietal bone near the postero-superior angle, lacks the usual translucency and is evidently of pathological origin, thus confirming the statement made by Greig (*loc. cit. supra*) that, "No case of unilateral parietal thinness appears to have been reported."

Professor Elliot Smith said that he disagreed with the view that the thinning of the parietal bone was congenital. The outer table is thinned, the diploë exposed and then eroded. The condition is due to some factor, such as pressure on the outer table causing its absorption. Among ancient Egyptian skulls it is found only during one period commencing at the 2nd Dynasty, and ceasing 1000 B.C. The individuals were of a rich class, who wore full-bottom wigs like a High Court Judge. Seventy cases were found in a single cemetery. In European Museums Sir George Humphry found only five. Among 17th-century old Irish skulls there was a considerable number of cases showing this condition.

The second specimen shown was simply a pathological case.

Mr Cave also exhibited a specimen of rudimentary first thoracic rib, a description of which will be published in the *Journal of Anatomy.*

(2) P. N. B. Odgers exhibited a specimen of bilateral superior vena cava, an account of which will be published in the *Journal of Anatomy.*

Professor Frazer, commenting on the absence of the left innominate vein, raised the question as to which was the primary condition, the absence of a cross branch, or persistence of the left superior vena cava. Odgers in reply stated that in 38 cases of the anomaly a cross branch was present; in these cases therefore the persistence of the left superior vena cava was not due to the absence of an anastomising branch.

(3) Professor Richard H. Hunter demonstrated "Two cases of congenital diaphragmatic hernia."

The first specimen was a cat showing a persistent left posterior pleuro-peritoneal recess through which passed the upper horn of the left uterine tube. The cat was in an advanced stage of pregnancy and the portion of the uterine

tube herniated into the thorax contained a foetal cat. There does not appear to be any specimen of this nature reported in the literature on the subject.

The second specimen showed a hernia of the stomach and part of the lesser omentum into the thorax through a greatly enlarged oesophageal opening in a female body, of 53 years, found in the dissecting rooms of Belfast University. The stomach lay in a true hernial sac of peritoneum, behind the pericardium opposite the 9th, 10th, 11th and 12th thoracic vertebrae. In a series of 34 cases of diaphragmatic herniae published by Sir Arthur Keith in *The British Medical Journal* of 1910, there is only one case through the oesophageal opening.

(4) Dr BEATTIE read a paper on "Diaphragmatic hernia in Primates."

He discussed the incidence of diaphragmatic hernia amongst lower animals and stated that in the past two years at the Prosectorium of the Zoological Society of London 674 mammals died and autopsies were performed on all these. During that time only three cases of diaphragmatic hernia were seen. Two of these were in animals of the family Felidae and the other animal was a small squirrel monkey.

With such small numbers it would be useless to draw any definite conclusions but several points of interest were noted. All the cases of diaphragmatic hernia were of the "pleuro-peritoneal" type, i.e. the viscera passed into the thoracic cavity through the pleuro-peritoneal opening. An examination of the diaphragms of all Felidae dying in the Menagerie disclosed the fact that in many of these animals a definite hiatus was noted between the crural and costal parts of the diaphragm. The peritoneum was separated off from the pleura by some areolar tissue. This hiatus although by no means constant (it occurred in five specimens out of twelve animals (Felidae) which were examined) varied from a slit-like opening a few millimetres wide to a triangular opening nearly a centimetre in greatest length and four millimetres wide. All were on the left side.

During the years 1925 and 1926, 271 Primates died in the Gardens and only one case of diaphragmatic hernia was found. The Primates dying during 1926 (137 animals) were examined for signs of diaphragmatic defects. In this series three animals showed gaps, between the muscular segments, which could be regarded as abnormal in size. Again all these gaps lay on the left side and in the region of the pleuro-peritoneal opening. One was found in a young chimpanzee, another in a common macaque monkey and the other in a green cercopitheque. In none of these did the defect measure more than two centimetres in length and six millimetres in width at the base. They were all triangular in shape.

Diaphragmatic hernia in the Primates (excepting Man) is very rare. The site of the point of greatest weakness in the diaphragm is at the left pleuro-peritoneal opening. This opening has not been found in any normal primate but three cases have been seen where the opening has been closed but no more. No parallels to the other forms of diaphragmatic herniae (as summarised by Sir Arthur Keith) described in Man have been found.

In the antelopes the fibres of the central tendon may show wide spaces between some of the interlacing fibres but a protrusion of the peritoneum into the gap has never been observed. In these animals weakness of the diaphragmatic sheet is very rarely seen in the region of the pleuro-peritoneal openings.

(5) Lady GRACE BRISCOE, introduced by Professor Lucas Keene, demon-

strated a case of hernia through the central tendon of the diaphragm in a cat, a description of which will be published in the *Journal of Anatomy*.

In the discussion of these cases Professor FRAZER commented on the relation of these anomalies to the development of the pleural cavities, and the closing off of the pleural from the pericardial and peritoneal cavities, which was a very complex process and not yet fully understood.

Mr MCADAM ECCLES said that he had three cases of diaphragmatic hernia. One clinical case died after an exploratory operation. In 37 cases which he had investigated in addition to these three, hernia through the pleuro-peritoneal opening was the most common. In a case at St Bartholomew's Hospital, which might be described as para-oesophageal, the hernia was enclosed in a retropericardial sac. A considerable number of cases occurred through the left dome of the diaphragm, but hernia through the central tendon was rare.

Professor HUNTER demonstrated the manner in which kyphosis of the vertebral column by traction and stretching of the diaphragm would favour the development of a diaphragmatic hernia.

Dr J. BEATTIE stated that in the Zoological Gardens marked thinning of the diaphragm had been observed in antelopes and other mammals, which would predispose to the production of diaphragmatic hernia in these animals.

(6) Mr HAROLD C. EDWARDS demonstrated a case of congenital subluxation of both shoulder joints, a full description of which will be published in the *Journal of Anatomy*.

(7) Mr CECIL P. G. WAKELEY showed a "double gall-bladder" removed by operation from a woman aged 56. There were two distinct gall-bladders with their own cystic ducts; the smaller of the two sacs contained numerous stones, while the larger contained none.

Anomalies of the gall-bladder are of rare occurrence yet several have been described. These range from the condition of complete absence to the presence of multiple gall-bladders. From the developmental standpoint one would expect a larger percentage of abnormalities since the gall-bladder is developed as an outgrowth from the primary hepatic diverticulum. This outgrowth is sometimes bifid giving rise either to complete division into two, or subdivision of the fundus.

The first recorded case in which a double gall-bladder was removed at operation was that of Sherren, who in 1910 operated upon a woman aged 25 and removed the specimen (No. 561.31) which is now in the museum of the Royal College of Surgeons of England.

(8) Doctor L. R. SHORE gave a demonstration of congenital abnormalities of the upper limb, a full description of which will be published in the *Journal of Anatomy*.

(9) Mr D. STEWART showed lantern slides of microscopic sections illustrating the innervation of the dentine; an account of which will appear in the *Journal of Anatomy*.

(10) Professor LE GROS CLARK read a paper on the "Brain of a gorilla," which is published in this part of the *Journal of Anatomy*.

Professor ELLIOT SMITH commenting on the question of right- or left-handedness which arose from the description of the above case stated that variations occurred in this respect. The statement has often been made that

gorillas and chimpanzees are ambidextrous, they are however sometimes left-handed, and the Ourang is usually right-handed.

(11) Miss ALICE BLOOMFIELD and Professor FRAZER gave a communication on the "Formation of the lower end of the vagina and the hymen." This paper will be published in full in the *Journal of Anatomy.*

Dr HOPKINSON asked whether the hymen was peculiar to Quadrumana. It was stated that Dr Berry Hart had described remnants of the hymen in most mammals.

Professor FRAZER said that the Müllerian ducts were entirely responsible for the formation of the vagina, and that there was no bulbous formation at the lower ends of the Wolffian ducts.

(12) Dr R. H. ROBBINS demonstrated two specimens of arterial abnormalities. The paper will be published in the *Journal of Anatomy.*

(13) Miss IDA C. MANN presented a paper on "The differentiation of the human retina."

A demonstration of the development of the nuclear layers of the human retina from the neuro-epithelium of the wall of the optic cup was given with the aid of a series of sections from human embryos ranging from 4·5 mm. to term. In the early sections the inner layer of the optic cup was seen to consist of a nuclear and a marginal layer only. At about 12 mm. displacement of nuclei into the marginal layer was commencing, leading (at 17 mm.) to the formation of an inner neuroblastic layer separated from an outer neuroblastic layer by the transient fibre layer of Chievitz. From the inner neuroblastic layer were developed the ganglion cells of the retina, the amacrine cells and the nuclei of the fibres of Müller, and from the outer neuroblastic layer the bi-polar nuclei, the horizontal cells and the nuclei of the rods and cones. The process was complete over most of the retina (excluding the macular and anterior regions) before the 8th month. It was also pointed out that in early stages (4–7 mm.) the lower portion of the wall of the optic vesicle shared in the capillary vascularisation common to the surface of the whole of the developing central nervous system. This vascularisation is transient in the wall of the optic cup, disappearing after 7 mm., and is followed at a much later stage (100 mm.) by the development of the arteria centralis retinae from the hyaloid artery where it passes through the optic disc.

(14) Miss IDA C. MANN read a paper on the development of the "third nerve nucleus," which is published in this part of the *Journal of Anatomy.*

APRIL, 1927

A CONJOINT meeting of the Association des Anatomistes and the Anatomical Society was held in University College, London, on Monday, Tuesday and Wednesday, April 11th, 12th and 13th. The chair was taken on Monday, April 11th by the President of the Anatomical Society, Professor ELLIOT SMITH, and on the two succeeding days by the President of the Association des Anatomistes, Professor BRACHET.

(1) Professor J. T. WILSON made communications on:

(1) "The question of the constitution of the early blastocyst of cavia."

(2) "Maternal haemopoiesis in the rat placenta."

Both papers will be published in full in the *Journal of Anatomy.*

(2) Professor LAGUESSE (Lille) read a paper "On the first stages of histogenesis in the umbilical cord of the human embryo."

The mucous tissue, like general loose connective tissue, presents lamellae. In an embryo of 15 mm. a certain number of long lamellae, at the periphery of the umbilical cord, are radially disposed like those of Selachians. They were also found in an embryo of 55 mm., but at this stage the lamellae are shorter. New lamellae are continually being formed by the exoplasmic transformation of the aliform extensions of cells. The fibrils always appear in the substance of the lamellae.

(3) Professor TUMA (Prague) read papers on:

(1) "The protective apparatus of the placenta in the rabbit."

The author had studied the penetrability of the rabbit's placenta for substances either innocuous or injurious by means of intra-vitam injections of Kiyono's lithium-carmine and arrived at the conclusion that the carmine does not penetrate the membranes of the embryo. The elements that retain the carmine in the placenta are the endothelial cells of maternal capillary vessels. The formation of the granules of carmine in the endothelial cells corresponds directly to the tension of the oxygen penetrating the wall of the vessel in this place. The relatively low tension of the oxygen in the tissues of the embryo is according to the author's opinion the direct cause of the fact, that the embryonal tissues and cells do not take the carmine from maternal tissues.

(2) "On the histology of the interstitial cells of the human mammary gland."

The author came to the conclusion that the interstitial cells in the human mammary gland are lymphocytic plasmocytes, which, in contrast to similar cells in animals, are comparatively rare, and in certain periods of activity of the mammary gland contain in their cytoplasm granules having specific staining qualities. The granules are gradually formed during pregnancy, reach their maximal quantity in the first days of lactation when they crowd the interstitial cells. During lactation they decrease again. In the case of older multiparae there are found, as a residue from previous lactations, some interstitial cells with granules in the inactive mamma, which otherwise contains in the stroma typical plasmocytes only. These plasmocytes are constantly to be found in the mammae of children and before the first lactation. The granules of the interstitial cells are according to the author's opinion an accumulation of milk vitamins.

(4) Professor WINIWARTER (Liége) read a paper on "The intimate phenomena of parasyndesis." The author has, for the first time, described the mechanism of chromatin-reduction as a parallel coupling of chromosomes (parasyndesis). He now attempts to study what happens during this coupling. Some authors believe that the homologous paternal and maternal chromosomes always remain distinct; others (Jansens) that the chromosomes exchange portions of their substance, during a complex phenomenon known as "chiasmatypie."

Recent studies of spermatogenesis of *Gryllotalpa vulgaris*, demonstrate the existence of a short, but actually existing stage, in which the coupled threads are fused together, probably after interchange of the chromatin particles. The new duality, which occurs later, results from a reorganisation of the chromatin

bodies, which were previously ranged in two parallel rows. When compared with gonial mitosis this phenomenon is absolutely different: on one side (gonia), exact division into two identical halves; on the other (cyte) irregular distribution of granules in two threads which are never symmetrical.

From this it follows that the chromosomes which are divided at the first maturation-division are probably very different from those which were coupled during parasyndesis. On the other side "chiasmatypie" is not proved, nor even necessary to explain the interchanges which occur between homologous chromosomes.

(5) A paper by Dr MAX ARON (Strasbourg) on "The rôle of the central nervous system in the growth of the tadpole" was read by Professor BENOIT.

In the tadpole there is a centre of growth which is situated between the mid- and hind-brain. From this centre there emanates a certain influence which excites growth, and which travels along the spinal medulla in the cranio-caudal direction. If the continuity of the spinal medulla is interrupted, the growth of its posterior segment is retarded. The correlation of growth between the different segments of the body depends on this influence, which diffuses along the spinal medulla. The author demonstrated the co-operation of this phenomenon with other factors, e.g. blood supply, or peripheral innervation, which influence the phenomena of growth.

(6) Dr E. CRACIUN (Paris) read a paper on "Epithelial movements in tissue cultures and stereotropism."

The formation of a membrane of the fourth type (Lewis and Lewis) in epithelial cultures affords a good opportunity to study the movements of epithelial cells. This formation occurs in two different stages. During the first, the cells grow out and form arches and rows; in so doing, the cells are manifest as free, independent elements, exhibiting active and polarised movements. The cells seem to move mainly by sliding (cytolisthesis) on the surface of another cell or of any formed material. Before moving, the cells need the contact of a solid phase, to which they show a positive thigmotactic reaction, i.e. these cells become partially flattened out and adhere to the solid. Under these conditions only are the cells able to move by chemiotropism cytotropism, etc.[1].

In the second stage, the arches form a continuous membrane. This last form is maintained by an epithelial culture so long as no connective tissue cells grow in it. In order that the membrane may persist and develop, the peripheral cells show active amoeboid movements, while those in the central part of the membrane are in a partial state of quiescence. Active cellular movements are therefore manifest during this second stage also.

The two different stages can be easily observed in slowly growing cultures, forming either a free membrane or one surrounding the explant.

It is rather difficult to observe the epithelial cell in the isolated state because of (1) its origin from highly differentiated tissues, (2) the rather complex conditions occurring in tissue cultures, (3) the very short time during which the cultures ordinarily show a "first stage," (4) the very strong cytotropism (W. Roux) of the epithelial cells.

(7) Dr A. S. PARKES read a paper on "The effects of exposure to X-rays on the ovary of the mouse in relation to the oestrous cycle," an investigation carried out in conjunction with F. W. R. BRAMBELL and UNA FIELDING.

[1] Stereotropism is therefore only an indirect cause of cellular movement.

X-irradiation of the ovary of the mouse at all ages, if adequate, results in the destruction of all the oocytes and the disappearance of follicles as such. The sterilised ovaries, after irradiation, are composed chiefly of tissue derived from the germinal epithelium in the case of immature animals, and when adult, from the epithelial elements in the cortex. Corpora lutea, present at the time when the ovary was irradiated and those formed afterwards from atretic follicles, persist indefinitely in the sterilised ovary but have no effect on the oestrous cycle. Small anovular follicles are often formed after irradiation.

The oestrous cycle of the accessory organs of animals with sterilised ovaries, in which no follicles or other rhythmically developing structures are present, is physiologically, histologically and statistically indistinguishable from the normal. It is suggested that the oestrous producing hormone ("oestrin") is produced continuously by the ovary independently of follicular maturation and that it periodically attains a threshold value, thereby accounting for the oestrous rhythm.

(8) Professor DALCQ (Brussels) read a paper on "The respective rôles of the hyaloplasm and the chromosomes of the sperm nucleus in fertilisation."

The spermatozoids of *Rana fusca* are treated before fertilisation with trypaflavine, following the method of G. Hertwig. The cytological study of the fertilised eggs shows that after sufficient intoxication the chromatic part of the male pronucleus goes entirely into one of the first blastomeres and is resorbed in the cytoplasm after a few mitoses. If such intoxicated spermatozoids are used for experimental polyspermy, centrospheres entirely deprived of chromosomes or of any chromatic substances make their appearance. Such centrospheres are capable of some bipolar divisions. It was thus found that while *pure* cytasters, obtained in experimental parthenogenesis are unable to divide (Fry), *pure* centrospheres derived from segmentation mitosis are capable of dividing several times. The reason for this difference appears to be that these centrospheres have received a *part of the living hyaline nuclear sap*, which contains the principle responsible for the subdivision of the asterian gelations. But the experimental dissociation between chromosomes and nuclear sap can, at least under the conditions in which the researches are carried out, be temporary only. Mitoses with chromosomes are more powerful than the achromosomal ones, and a conflict arises which causes the latter to disappear.

(9) Professor GRYNFELLT (Montpellier) read a paper on "Experimental studies on the method of formation of collagen connective tissue in scars."

Attention was drawn to certain facts concerning the origin of scar tissue destined to replace the loss of material created by abscesses containing streptococci in the guinea-pig. Mention was made of an investigation carried out in collaboration with H. J. Guibert in which it was shown that the granulation tissue of the so-called pyogenic membrane functions as a phagocytic apparatus and also as a *fibrogenic zone* of which the primordial element is a syncytium formed by the fusion of histiocytes (or macrophages). On the surface of these protoplasmic trabeculae an exoplasmic covering which sometimes spreads out in lamellar prolongations is differentiated. The first indication of the connective tissue net, in the form of delicate fibres (trabeculae), appears in this exoplasm. Two layers may be distinguished in the fibrogenic zone, an internal purely syncytial and devoid of blood vessels and an external fibrous layer corresponding to the syncytial region which is now invaded by

newly-formed vessels. These advance regularly, and as a result of chemical modifications which they cause in the exoplasm, trabeculae appear around them following a line of fibrillation which recalls the line of ossification in the cartilage of diaphyses and epiphyses. This newly-formed tissue in the purulent cavity enters very slightly into the constitution of the scar which is derived in large part from hyperplasia of the connective tissue network at the expense of the lacunae of the lamellar tissue, a kind of very dense fibrous tissue of alveolar structure being formed.

(10) Miss Hope Hibbard (Paris) read a paper on "Oogenesis in certain teleosts with special reference to the chondriome, vacuome, and yolk formation," an investigation carried out in conjunction with Professor Parat.

During a study of oogenesis and vitellogenesis in the perch and in the stickleback, some interesting facts relative to the Golgi apparatus or vacuome and the mitochondria have come to light. The inter-relations of these cell structures and the confusions arising from misinterpretation, merit an explanation of our method of procedure in identifying these bodies. Purely morphological aspects of cytology are extremely important as a base for studies on functional significance. Lacking clearness on these fundamental points, numerous authors have launched forth on discussions of the rôle of the Golgi apparatus without having accurately determined that it was in reality the Golgi apparatus with which they were dealing.

The two Teleosteans used in this study of the development of the egg were the perch (*Perca fluviatilis* L.) and the stickleback (*Pygosteus pungitius* L.). In the case of the perch, all the eggs to be laid in the spring develop simultaneously during the early months of the year. All other oocytes in the ovary remain in a quiescent stage at a given point in their development until the following season. The stages from the earliest primordia up to the quiescent period can be recognised in the folds of the ovarian epithelium, but between this period and maturity large numbers of eggs in only one stage of vitellogenesis are found in any one animal.

The mitochondria of the young perch eggs are easily demonstrated by the usual methods of fixation and staining used for these elements. The best results follow fixation by a modified Dietrich (M. Parat) method, and staining by Altmann-Kull. They are also easily stained post-vitally by Janus green; and the cytoplasm of living eggs when examined by darkfield illumination is seen to be so crowded with refractile mitochondria that it presents a fibrillar structure. During the initial stages of development the mitochondria present the series of changes often described in young oocytes. In the earliest stages examined, the nucleus is completely surrounded by very small granules and filaments regularly distributed over its entire surface. Shortly afterwards the mitochondria become clearly polarised on one side of the nucleus, forming a mass of entangled filaments. This is the stage of the Balbiani corpuscle. From this central mass, filaments migrate out and are gradually disseminated throughout the cytoplasm. This regular distribution is soon modified by the appearance of a perinuclear zone where diffusions from the nucleus seem to push away the formed elements of the cytoplasm. The result is an accumulation and concentration of mitochondria in a spherical surface concentric with the nuclear membrane but at some distance from it. There is also a concentration in this region of the vacuome of the cell. It is in this condition

that the oocyte remains for an indefinite period until the formation of the yolk commences.

In an effort to identify the Golgi apparatus or vacuome of the cell, the classical impregnations by silver nitrate and osmic acid were made, following fixation in the fluids of Cajal, Da Fano and Champy. The results were particularly good after staining with silver nitrate, where the cytoplasm was found crowded with batonnets and half-moons. It would be difficult to imagine a more clear-cut case of the so-called dictyosome form of Golgi elements. But before drawing final conclusions, careful studies of vitally stained ovaries were made. This was accomplished either by injection of neutral red into the peritoneal cavity of the living fish and subsequent examination, or by immersing an entire ovary in physiological salt solution containing neutral red for some minutes. Nothing corresponding to the dictyosomes could be coloured by neutral red. Moreover, fixations were made by the methods of Cajal and Da Fano at a temperature of zero, during twenty-four hours of fixation. Following this treatment the cytoplasmic changes due to cytolysis were slight, and the impregnation now showed not dictyosomes but filamentous mitochondria of the character already demonstrated by the specific mitochondrial techniques. All intermediate stages from normal slender filaments through vesiculated filaments with swellings or blebs and occasional fragmentation, to the isolated "dictyosomes" were found, depending on the excellence of the fixation. All were blackened by silver nitrate. The obvious conclusion is that all are mitochondria in various stages of preservation.

The vacuome or true Golgi apparatus was clearly visible by vital staining with neutral red. Its history is, to some extent, parallel to that of the mitochondria. There is a condition of polarisation of the Balbiani-corpuscle where it is seen in the form of discrete droplets caught in the meshes of the mitochondrial felt-work. Then the vacuoles become disseminated through the cytoplasm and increase in size. These fragment into large numbers of much smaller droplets which finally accumulate near the nucleus. In the resting stage they are mingled with the mitochondria concentrated in the perinuclear zone indicated above.

Following the observations on the living egg, further attempts to impregnate the Golgi apparatus by osmic acid proved successful. The Mann or Champy fixation followed by a long impregnation (about 20 days) gave excellent results, and by counter-staining with Altmann's acid fuchsin, the Golgi bodies in black, and the mitochondria in red, were clearly visible in the same eggs.

Great emphasis should be laid upon the importance of vital staining as a check on methods of fixation. Without it, in this case, we should certainly have concluded that the vesiculated and fragmented mitochondrial system represented the Golgi apparatus in the egg of the perch.

The appearance of the impregnated vacuome after the Mann-Weigl technique may vary somewhat. If the impregnation is heavy the entire vacuole appears uniformly black. If it is less deeply impregnated, the surface only of the vacuole is black, giving the appearance in sections of rings or crescents. Apparently the reduction product of the osmic acid is deposited first upon the interface between the watery contents of the vacuole and the cytoplasm with which it is immiscible. Later, if more and more reduction takes place, the vacuole is more and more filled and blackened.

The relation between the vacuoles and the mitochondria is very intimate, a condition not uncommon among other types of cells. Mitochondria (lipo-

protein substances) are seen ramifying among the vacuoles and even clinging by some sort of surface attraction to the surfaces of the vacuoles (aqueous substances). It would seem a very easy matter to confuse the two in making microchemical tests unless their spatial relations are clearly recognised.

In this connection mention should be made of some experiments made to test the findings of Ciaccio regarding the chemical constitution of the Golgi apparatus. Eggs fixed according to the first technique (II) of Ciaccio, showed bodies throughout the cytoplasm giving the lipoid reaction. These correspond to the false dictyosomes which have been shown to be badly fixed mitochondria. By modifying the temperature so as to accomplish the entire fixation at zero degrees, the lipoid reaction was positive throughout the now normal mitochondria. In both cases, the vacuoles, or Golgi apparatus, appeared as empty spaces, a result confirmed by the modified Dietrich technique.

After applying the methods recently published by Ciaccio (III) for demasking the lipoids, that is, breaking down the lipo-protein linkage so as to render the lipoids alone stainable by Sudan III, *the vacuoles remain, as before, empty spaces.* The entire perinuclear zone, where we have seen the vacuome localised and also the densely accumulated mitochondrial filaments, gives a diffuse lipoid reaction, except within the vacuoles, and it shows numerous granules or deposits which stain deeply. These are the products of the alteration of the mitochondria. Furthermore, throughout the rest of the cytoplasm lying outside this zone, the filamentous mitochondria can be distinguished; they are stained very slightly, but here and there along the filaments there appear masses or agglomerations of intensely stained lipoid material.

The demasking methods of Ciaccio prove, therefore, that there are no lipoids in the vacuoles or Golgi apparatus but that, as one of us (M. P.) has repeatedly affirmed, the existence of vacuoles in a delimited zone attracts a more or less intense concentration of lipoids on their surfaces. The process of demasking results in an accumulation of the lipoids in compact masses or granules. These lipoids are indicated, although in a defective fashion in the form of artefacts, after demasking; but in a more normal fashion they were already put in evidence by the older techniques. Since the morphology of the dense perinuclear zone containing both mitochondria and vacuoles has been carefully studied, we have no hesitation in affirming that the demasked lipoids are outside the vacuoles.

In the case of *Pygosteus*, the ovary presents all stages of development at one time, from the smallest oogonia to the oocytes, whose cytoplasm is already crowded with yolk plates. For this reason the study of the origin of the yolk is particularly fruitful in this animal.

The procedure used was similar to that described for the perch. The mitochondria follow a series of changes analogous to that seen in the first case. The polarisation of early stages is followed by general dissemination. Later the concentration due to pressure from the region of perinuclear diffusion is the same. After this period the formation of yolk commences. There is no indication that mitochondria are directly transformed into yolk. In fact at the beginning of vitellogenesis, the minute granules which grow into the yolk plates are all at the periphery of the egg, while the most concentrated mitochondrial zone is in the perinuclear region just outside the clear area occupied by nuclear diffusions.

On the other hand, the vacuolar system has a definite bearing on the development of yolk. From its perinuclear position the vacuome migrates

practically to the peripheral zone of the cytoplasm where the individual minute vacuoles grow directly into individual yolk plates. That is to say, the vacuolar contents becomes more and more concentrated by the accumulation of products absorbed from the cytoplasm until it is so dense at the end of the elaboration that the large yolk plates no longer can be stained with neutral red. They have passed out of the aqueous phase necessary for such vital staining.

The reactions to fixatives of the cytoplasmic constituents in the stickleback differ considerably from those in the perch. The entire history of the vacuome is put in evidence very clearly by the use of the Cajal or Da Fano silver impregnation methods, the same methods which gave only the chondriome in its normal or in its false dictyosome condition, in the case of the perch. The proof of the accuracy of this conclusion is found in the use of vital staining by neutral red. The same droplets in the cytoplasm stain by neutral red in the living egg that appear black after the use of Cajal or Da Fano's method.

The use of Mann-Weigl, which showed clearly the vacuome in the perch, shows only oil droplets in the stickleback. These oil droplets are quite visible in the living egg as faintly yellowish, refractive globules, not to be confused with the aqueous vacuoles which are coloured by neutral red in the same cells. They arise *de novo* in the mid-zone of the cytoplasm and grow continually in size. Throughout their history they are quite independent of both mitochondria and vacuoles, or Golgi apparatus.

The conclusion to be drawn from these observations on two Teleosts giving quite different reactions to the fixatives used cannot be insisted upon too strongly. In order to understand the cellular constituents, various methods of technique must be focussed upon the single object. Only by a comparison of the observations taken from many points of view can accurate interpretations be made. And perhaps the most important of these methods is that of vital examination.

(11) Professor PARAT (Paris) read a paper on "The behaviour of the vacuome during spermatogenesis."

(12) Mr R. J. LUDFORD read a paper on "The Golgi apparatus in relation to secretion."

At the onset of secretory activity in a gland cell, the Golgi apparatus hypertrophies, and spreads out in the cytoplasm, either in the form of a network, or as scattered bodies. The secretion makes its appearance in intimate relationship with the substance of the apparatus. Both in invertebrates and vertebrates, and in all types of glands, which have been studied, there is a definite relationship between the Golgi apparatus and secretion.

(13) Professor GATENBY read a paper on "The nature of the Golgi apparatus."

(14) Dr J. MOTTE (Montpellier) read a paper on "The value of the chondriome in green plants."

In vegetative cells of mosses, the chondriome is composed of amyliferous plasts and chondriosomes. But in the generating cell plasts leave their starch, appearing sometimes spindle-shaped, sometimes filiform. This is a proof of their plastic properties. In another critical period of life, i.e. spermatogenesis, all plasts are transformed into mitochondria, and now, it is impossible to distinguish the latter from the plasts. After 5 or 6 spermatogenic generations,

this homogeneous material is condensed into a quite homogeneous mitochondrial body producing in a part of it a grain of starch.

It seems impossible to admit, at least in this case, a double chondriome comprising two parts; an active one, and another inactive. It seems more probable that the chondriome is at first undifferentiated. Further, any part of it may become functional and may later return to the undifferentiated and homogeneous stage.

(15) Dr D. M. Blair read a paper on "A peripheral neural mechanism on capillaries of striate mammalian muscle."

Observations were made upon the nerve supply of capillaries in limb muscles of *Cavia*. Bielschowsky technique, suitably controlled to avoid impregnation of connective tissue, was employed; nerve fibres were sharply stained, while the transverse striations of muscle fibres and the outlines of capillaries stood out clearly. Small multipolar cells were observed lying upon the muscle fibres and closely associated with the capillaries. Certain processes of these cells appeared to curl round the muscle fibres, while others passed on to the walls of capillaries and in some instances could be traced into continuity with undoubted non-medullated nerve fibres. From their form and staining reactions these cells are believed to be neural, and it is suggested that the arrangement here described may form a peripheral neural mechanism correlating the calibre of the capillaries with functional activity of the muscle fibres.

(16) Professor H. H. Woollard read a paper on "The innervation of voluntary muscle."

The views on the morphology of the double innervation of striped muscle may be classified as follows:

(1) The interpretation of Boeke which suggests that each muscle fibre is doubly innervated (*a*) by a cerebro-spinal fibre, and (*b*) by a postganglionic sympathetic fibre, the terminal apparatus of the two systems standing in close relationship with each other.

(2) The view revived by the recent work of Kulschitsky which suggests that there are two kinds of muscle fibres, a thick and a thin, and two kinds of nerve fibres, a medullated and a non-medullated, innervating separately the two kinds of muscle fibres. The hypothesis has been further expanded to include for each fibre a corresponding sensory innervation.

(3) In this group may be included those investigators who doubt the theory of double innervation of either kind because no function can yet be assigned to the sympathetic innervation of striate muscle; those who accept the investigations of Boeke but would give them a different interpretation; and finally, those who deny the double innervation of striate muscles except in the case of the ocular muscles.

The author's observations include: a large variety of normal mammals; mammals suffering from deficiency diseases; cats in which the abdominal sympathetic chain had been wholly removed on one side; cats in which the ventral roots of the lumbosacral plexus had been divided on one side. The histological methods included the gold chloride method of staining; the silver method as modified by Boeke; and the intra-vitam methylene blue method. The latter gave the clearest pictures and further, the fibres could be followed for great distances in thin flat preparations.

The results have been entirely negative in regard to the double innervation either of the Kulschitsky type or of the Boeke type, *save in the case of the ocular muscles*. Owing to the resemblances to the ocular muscles presented by the lingual muscles and the diaphragm, special attention was given to them, but with negative results.

In the ocular muscles two distinct fibres were observed, one the ordinary medullated nerve fibre with the typical motor terminal plate, the other a non-medullated fibre ending in a grape-like termination. Each kind of nerve fibre was distributed to a separate muscle fibre. The muscle fibres were easily distinguishable as thick and thin, the thin being associated with the non-medullated fibres. These non-medullated fibres are in the light of the experimental results of Sherrington and Boeke believed to be sympathetic fibres. Comparison with Dogiel's description and figures suggest that they have nothing to do with the sensory fibres in the eye muscles. Comparison with the published figures of Boeke on the eye muscles suggest that they are identical with his non-medullated fibres. If this be true then they behave not according to the Boeke idea but according to the Kulschitsky description.

(17) Professor E. S. Goodrich read a paper on "The problem of the sympathetic nervous system from the morphological point of view."

The autonomic or sympathetic system may, in a wide sense, be here defined as consisting of excitor and motor neurons connected with the central nervous system by outflows of efferent preganglionic fibres. In the higher vertebrates the physiologist subdivides it into (*a*) sympathetic proper or thoracico-lumbar outflow; and (*b*) parasympathetic or mid-brain, hind-brain, and sacral outflows (including the peripheral neurons so supplied).

But what strikes the morphologist is that some of these outflows or preganglionic fibres pass through dorsal (posterior) nerve roots, and others through ventral (anterior) nerve roots. The whole system may be subdivided into (*a*) the dorsal-root system (hind-brain outflow); and (*b*) the ventral-root system (mid-brain, thoracico-lumbar, and sacral outflows).

The problem then arises: How has the latter system been evolved? How have "sympathetic" neurons come to be connected with the central nervous system through ventral roots?

The connexion through dorsal roots (as in the cranial nerves of the hind-brain) appears to be the primitive one. In lower vertebrates, such as amphioxus and petromyzon, the ventral roots throughout the body supply the myomeres only. Any efferent fibres belonging to or representing the "sympathetic" supply to the viscera or skin must, in these forms, pass out through the dorsal roots not only in the head but throughout the whole length of the body. This condition persists in the hind-brain region of the higher forms, where the facial, glossopharyngeal, and vagus nerves represent the dorsal roots (of three segments) which remain separate from their corresponding ventral roots (abducens, and hypoglossal). Moreover, embryology shows that in the head, and probably also in the trunk region, most if not all the sympathetic neurons pass out along the dorsal roots. The evidence on this point, however, is still somewhat conflicting.

Clearly the evidence as a whole points to the autonomic system having been originally related to the dorsal roots, and we have to explain how in the higher vertebrates neurons belonging to the mid-brain, thoracico-lumbar, and sacral outflows acquired a connexion with the central nervous system by means

of preganglionic fibres issuing through the ventral roots. That is the problem before the morphologist.

(18) Professor CELESTINO DA COSTA (Lisbon) read a paper on "New observations on the evolution of the cranial ganglionic crest in mammals."

Adelmann has recently published in the *Journal of Comparative Neurology* a memorandum upon the cranial neural crest of the rat. He criticises my interpretation of the presence of certain cells in the region of the optic fossa in early embryos, as being an anterior prosencephalic neural crest. He believes that these cells are merely mesenchymatous and that the formation of a prosencephalic neural crest does not exist. I have once more examined his preparations and found that in the guinea-pig this cell-proliferation on the margin of the optic fossa, in the angle between the neural plate and the epiblast exists in several embryos from the stage of 6 somites until that of 10–11 somites. The cells of this anlage are well characterised, they are apparently larger and darker than the cephalic mesenchymatous cells. In the slides where the two kinds of cells exist side by side it is very easy to identify them. In shape and structure they are exactly similar to the cells of the genuine ganglionic crest of the trigeminus. The only explanation I can give of their formation is to consider them as a special proliferation of the cells at the margins of the neural plate in this region. The fate of these elements is very difficult to determine. In more advanced embryos it is very easy to find them encircling the optic vesicles, and their contact with the epiblast of this region is often seen. In advanced stages these cells mingle with the head mesenchyme and it is impossible to distinguish them. If a true mesectoderm exists, these elements might be considered as belonging to it. But as Brachet, Adelmann, the writer and others have pointed out, the ectoblastic region of the head mesenchyme is not yet proved, at least in mammals. The mesenchymatous nature of these elements is not admissible. They appear at a point where no mesenchyme exists at the time and their connection with the cells of the neural plate is incontestable.

(19) Dr R. M. MAY (Paris) read a paper on "Modifications of nerve centres due to the transplantation of the eye and olfactory organ in anuran embryos."

Homoio-transplants of embryonic eyes and olfactory organs in the otic region of embryos of *Rana temporaria* and *Bufo vulgaris* develop synchronously with these organs in the host. Thus the formation of a lens, optic nerve, visual cells, and retinal layers of the grafted eye takes place at the same time as the formation of these parts in the normal eyes of the host. This synchronicity of development is apparently the result of an external factor, perhaps hormone-like in nature. The grafted organs persist after metamorphosis.

There is a marked affinity of the optic neuroblasts for the neuroblasts of the central nervous system; this phenomenon may be called *neuroblastotropism*.

The optic nerve, even at the first stages of its formation and connection with a cranial ganglion, determines a hyperplasia of the latter. The nerve of a transplanted sensory organ that merely goes through a cranial ganglion causes no hyperplasia of this ganglion. But when it penetrates a cranial ganglion it determines a hyperplasia which varies from 28·4 to 78·9 %. The connection of a transplanted eye with a cranial ganglion across the macula acustica of an ear which was not excised also determines a ganglionic hyper-

plasia. Where a few axons merely penetrate into a cranial ganglion the resulting hyperplasia is small (13·7 %). Thus, the hyperplasia of a ganglion due to its connection with a sensory organ by means of the latter's nerve is a function of the number of fibres which penetrate into the ganglion. The force of attraction exercised by a nerve centre on a sensory organ may deform the latter.

A piece of telencephalon, grafted along with the sense organs, retains its anatomical individuality. Such a fragment of telencephalon attracts the optic nerve of grafted eyes and the cells of cranial ganglia. In the case where a piece of grafted telencephalon becomes fused with the medulla, these two parts of the central nervous system retain their normal architecture.

The penetration of an embryonic optic nerve into the medulla determines a migratory avalanche of the medullary cells about it. The connection of the nerve of a grafted olfactory organ with the medulla determines in it a hyperplasia (4·26 %) and a cellular migration towards the entering nerve. The medullary hyperplasia appears to be in direct relation, as to its magnitude, with the number of penetrating axons. When the medullary hyperplasia is very large (24·61 %), it reflects back on the medullary cells and fibres, caudally to the connection.

The pia-mater is a barrier which is crossed with difficulty by axons coming from grafted sensory organs.

The excision of the embryonic eye and olfactory organ usually causes no morphological change in the central nervous system. In some cases however, the diencephalon and telencephalon react by neoformations. These neoformations are totally different from the hyperplasias due to connection with the sensory organs.

These results constitute an additional proof of the theory of neurotropism of Ramón y Cajal and the theory of neurobiotaxis of Kappers. They are discussed at length in the *Archives de Biologie*, fasc. 3, 1927.

(20) Professor G. Leboucq (Ghent) read a paper on "The relation between weight and cortex of the human brain."

(1) In the adult brain, there is a fairly constant relation between the weight of the hemispheres and the cortex.

(2) The frontal lobe, which from the biological standpoint is more recent, has proportionally to its weight, a relatively smaller surface than the older lobes, more especially the occipital one.

(3) The surface of a cerebral hemisphere of average weight, amounts to about 2·7 times the surface of a smooth sphere of the same volume as the hemisphere.

Professor Loth (Warsaw) read papers on "The necessity of organising an international bureau with the object of studying the soft parts of primitive races."

(1) The author stated that he had made the anthropology of soft parts an object of study for the past ten years, and he was publishing shortly a work embracing a complete survey of the subject.

A synthetical study of the anthropology of the soft parts has convinced him that results will never be satisfactory until there is a central administration and until common methods are agreed upon, otherwise the efforts of different investigators will result in the loss of energy and material.

He proposed that an international committee should be elected by the members of the Association des Anatomistes and of the Anatomical Society of Great Britain and Ireland. Representatives of nations which possess colonies and can contribute scientific material of coloured races to be chosen.

He suggested that such a committee should consist of 2–3 Englishmen, 2–3 Frenchmen, 1 Belgian, 1 Dutchman, 1 Italian, 1 Portuguese, 2–3 Japanese, 1 Chinese, 2 Americans, 1 representative of the Rockefeller Foundation and 1 Pole as the initiator of the scheme.

This committee should have the power to invite and convene all men of science who are interested in this investigation.

The duty of this committee should be:

1. To send enquiries to universities, hospitals, etc., of countries with coloured populations.

2. To apply to governments, academies, and scientific societies for money to carry on this work, in order to cover propaganda, journeys and all other expenses.

3. The committee should apply to the Institute of Intellectual Collaboration of the League of Nations, and demonstrate that the investigation of primitive peoples, most of whom are rapidly becoming extinct, is a complementary work of international hygiene, which is one of the aims of the League of Nations.

4. The committee should collect and publish all information connected with this investigation.

(2) "On the shortening of the trunk and of the thorax."

The author discussed the theory concerning the shortening of the vertebral column and of the thorax and pointed out some discrepancies. He alluded more particularly to the work of Tredgold, and stated that the view that the vertebral column and the thorax are undergoing shortening, *pari passu*, is an error. He demonstrated that the thorax of the *Lemurs* is half the length of the body only, while in the apes it reaches two-thirds of the body length. Consequently as the vertebral column shortens the thorax is undergoing a relative elongation. Simultaneously, the free part of the abdomen undergoes some interesting modifications.

(21) Dr E. P. Stibbe read a paper on "A comparative study of the nictitating membrane in birds and mammals."

General conclusion. The nictitating membrane of mammals differs greatly from that of birds, and is not homologous with it.

Demonstration.

(1) Dissections of nictitating membrane and its musculature in ostrich and duck.

(2) Dissections of these structures in calf, cat, etc.

In birds there is a definite special musculature—the pyramidalis and quadratus of Owen. In mammals the special mechanism is not obvious; the membrane is connected to the levator palpebrae and to other sheets of muscle in the "subperiosteal" plane.

(3) and (4) Serial sections of the membrane in the same animals, showing marked differences in structure.

Points about the mammalian membrane:

(*a*) It is essentially a cartilage rather than a membrane; the nictitating cartilage which evaginates the apparently unmodified conjunctiva.

(*b*) It is possibly a fixed structure, the eye moving under it, rather than it over the eye.

(*c*) Structure of the Harderian gland.

(22) Mr Denis Browne read a paper on the "Surgical anatomy of the tonsil" which will be published in full in the *Journal of Anatomy.*

(23) Dr Bellocq (Strasbourg) read a paper on "A contribution to the study of the temporal region of the cat."

The cat's temporal bone as well as the dog's temporal presents dissociated elements which differ very markedly from the morphological unity of the human temporal bone.

The squama, which has no posterior horizontal portion, the petrous element, which represents merely the osseous capsule but is better fixed than in the dog, and, finally, the tympanic bone reinforce the cranial wall; they are united by suture for a short distance externally and are distinctly isolated internally. These bones form an incomplete wall to the middle ear, in the constitution of which the great wing of the sphenoid still participates but in a more important manner than in the dog.

The following comparisons may be made: the wider participation of the sphenoid in the constitution of the middle ear in the cat seems to be correlated with the wider development, in the cat than in the dog, of the anterior part of the middle cerebral fossa. In the same way the direct participation of the deep surface of the squama in the delimitation of the middle cerebral fossa in the cat, from which it is eliminated by the sphenoid, and the parietal in the dog, seems also to be correlated with this wider development of the anterior part of the middle cerebral fossa. Moreover, when the feeble development of the petrous element and horizontal portion of the squama in the cat and the inability of the components of the temporal bone completely to enclose the middle ear are compared with the great development of the petrosal and the horizontal portion of the squama and the complete enclosure of the middle ear by the three components of the temporal bone in man, it will be evident that there is also a clear correlation of these peculiarities with the development of the brain, which differs very widely in the cat, dog and man respectively.

(24) Professor E. J. R. Evatt read a paper on the "Origin and morphology of the basement membrane," which will be published in the *Journal of Anatomy.*

(25) Professor Pires de Lima (Oporto) read a paper on "Duplicity of the anus and its significance."

I have had the occasion of studying two cases of double anus, the first in a four-year-old boy, and the second in a hen.

In both cases, only one of the orifices communicated with the rectum. The caecal apparatus of the hen was very complicated: it presented three parallel canals communicating with one another by means of valves. At the extremity of the caecum three diverticula were found.

I have also seen a double anus in a hen, possessing a supernumerary foot. Geoffroy Saint-Hilaire said that pygomelian monsters had usually two anuses. This was observed in the remarkable Portuguese monster Santos, described by Bland-Sutton under the name of "human tripod."

The author assumes the following hypothesis. Is not the duplicity of the anus (schistoprocty) an indication of double monstrosity?

Joly described under the denomination "Rhynodimy" a double monster whose monstrosity was localised to the nose.

Le Double described a woman of the same kind whose skull is in the Museum of the Faculty of Medicine of Montpellier.

If, in the cephalic extremity, there can be such a rudimentary double monstrosity, are not cases of duplicity of the anus an indication of double monstrosity affecting the opposite extremity of the trunk?

(26) Professor LUCIEN (Nancy) read a paper on "The significance of the superior bronchus of the right lung in man."

The first collateral of the stem-bronchus of the human right lung (Aeby's eparterial bronchus) is not a simple but a composite bronchus. It should be placed neither in the ventral series of bronchi, nor in the dorsal.

It may be termed a superior bronchus of the right lung and trifurcates into (*a*) a superior ventral lobar bronchus, (*b*) a superior dorsal bronchus, and (*c*) an apical bronchus or highest pulmonary bronchus. The superior lobe of the right lung is thus divisible into three lobar territories: (*a*) the superior ventral lobe, (*b*) the superior dorsal lobe, and (*c*) an apical lobe placed between the two preceding. These three territories can abnormally be indicated by the appearance of supplementary fissures.

There exists in the left lung also a superior bronchus which is identical with the corresponding one in the right lung and which is distributed in a similar manner in the superior region of the left upper lobe. It is a branch from the stem bronchus, but has a stem common to it and the first ventral bronchus.

In conclusion, the superior region of the two lungs in man presents a structure which in the main is comparable.

(27) Professor FRAZER read a paper on "The formation of the pleural sacs in man." This paper will be published in the *Journal of Anatomy*.

(28) Mr V. E. NEGUS read a paper on "The function of the epiglottis."

The epiglottis appears to be present in order to preserve the integrity of the olfactory sense when the mouth is open. It carries out this function by coaptation to a long soft palate, thereby preventing entrance of air by the mouth and ensuring the passage of a large current of air over the epiglottic mucous membranes.

An epiglottis is not necessary for purposes of deglutition, respiration, or phonation. In certain animals, however, it serves a secondary function during the swallowing of liquids and semi-solids, and it can also be of assistance in respiration.

In man the epiglottis is fairly large, but it is immobile, and does not come into contact with the short and degenerate soft palate. Therefore, when the mouth is open the greater part of the air stream passes through the mouth and not through the nose, and the olfactory sense is particularly feeble at such a time. It is found that all animals which are macrosmatic have an efficient epiglottis, which is able to come into contact with a long soft palate, while of the microsmatic species, many show degeneracy of this mechanism.

(29) Dr F. DAVIES read a paper on "Normal cholecystography."

When a number of radiograms of the gall bladder are examined after the administration of certain dyes, it is found that the characters of the shadows vary in different individuals. The object of this investigation was to determine if the characters of the gall bladder shadow of an individual had any relation to the type of bodily habitus of that individual. With this view, 100 students

were each given 5 grams of sodium tetra-iodo-phenol-phthalein by the mouth in gelatine capsules freshly coated with stearic acid, and radiograms of the gall bladder were taken 14½ hours afterwards. The students were classified after the manner of Mills into the following types of bodily habitus: Hypersthenic, Sthenic, Hyposthenic and Asthenic. From the cholecystograms the following deductions were drawn:

1. The length of the gall bladder shadow is not definitely related to the type of bodily habitus.

2. The maximum breadth of the gall bladder shadow is greater in the "better" types of bodily habitus, i.e. in the hypersthenic and sthenic types.

3. Both the neck and the fundus of the gall bladder shadow lie at a higher level and at a greater distance from the mid-line of the vertebral column in the better types of bodily habitus.

4. The rate of emptying of the gall bladder was estimated by noting the extent of reduction in the size of the shadow 2 hours after a fatty meal, which was given immediately after the first radiogram, and it was found to be quicker in the better types of bodily habitus. As gastric motility likewise varies with the type of bodily habitus, being fastest in the better types (Mills), a definite correlation is established between bodily habitus, gastric motility and the rate of emptying the gall bladder.

In this investigation it was noted that of 15 students who failed to give a shadow on the first investigation, 9 gave a good shadow when the investigation was repeated a few weeks later, using precisely the same technique. Also 2 students who gave a good shadow on the first investigation failed to give a shadow on repeating the investigation with the same technique some time later. This is important as most investigators declare that the absence of a gall bladder shadow with a reliable technique is certain evidence of disease of the biliary tract. The above evidence signifies that the factors which are essential for the production of a positive cholecystogram may be liable to physiological variation, and thus it appears that a negative cholecystogram *per se* (i.e. in the absence of clinical evidence of disease) is of less diagnostic value and significance than positive cholecystographic evidence of disease of the biliary tract.

(30) Professor LUCIEN (Nancy) read a paper on "The prenatal growth of endocrine organs in man." An investigation carried out in conjunction with Dr GEORGES.

The ponderable increase of endocrine organs during the foetal period can be represented by a curve comparable in its *ensemble* to the general curve of development of the body, without being exactly superposable.

The curves indicating absolute weights only show, indeed, a progressive augmentation of these weights which becomes more marked as birth is approached.

The study of the relative weights and of the curves designed therefrom, permits one to specify the conditions which exist between the general development of the body and the particular development of the organs.

The endocrine glands (hypophysis, adrenal bodies, thyroid gland and liver) early acquire their maximum relative weight. The liver and the hypophysis attain their higher relative weight in the first and second month, the adrenals in the fourth month and the thyroid gland in the fifth month. The liver and sometimes the thyroid gland maintain a higher relative weight until adult

life is reached but the relative value of the hypophysis and of the adrenal bodies falls progressively from the third month for the former and from the fifth for the latter.

These observations draw attention to the functional and anatomical importance of endocrine glands during prenatal life and show that they probably play a very early active rôle, and take part in the developmental processes of the body. Further, these observations supplement the conclusions which have already been drawn as the result of histological and physiological investigations.

(31) Professor Livini (Milan) read a paper on "Glycogen in the human embryo and foetus."

I have been for a long time engaged in researches on the histogenesis of the organs of the human embryo and foetus on physiological lines, with a view to determining the moment at which the organs in process of development have attained a structure comparable to that which they will have when fully developed, so as to warrant the supposition that when the organs have attained such a structural stage they are capable of performing their functions. I believe that by following this method it will be possible, when the researches are complete, to determine, by a comparison of the various organs—though perhaps only to an approximate degree—the reciprocal relations not only of their development but also of their functional powers.

Reference may be made to observations made upon a large number of human embryos and foetuses—from embryos of 12 mm. to foetuses at birth—in relation to their demeanour and to the distribution of glycogen in them.

The method adopted was that suggested by Vastarini-Cresi, other methods being also used for checking purposes.

Conclusions. The glycogen appears in the liver towards the end of the second month of intrauterine life (embryos of 38 mm.). It is present much earlier (towards the beginning of the second month—embryos of 13 mm.) in other parts, the epidermis, the myocardium, the myotomes, etc. in which it grows rapidly in quantity, and also appears in many other organs before it appears in the liver.

Since in the process of development a great many organs contain glycogen, not only at the time when the glycogenetic activity of the liver is nil, or at least very slight, but throughout the period of intrauterine life and even at birth—when the glycogenetic function of the liver is extremely active—I believe that a large reserve of glycogen is required for the embryo in process of development, probably in order that it may not suffer from any deficiency of sugar in the blood of the mother, thus rendering necessary the participation of other organs in glycogenetic functions. I do not think that these organs function vicariously for the liver and the voluntary muscles, which at their full development show the largest deposits of glycogen.

In relation to the content of glycogen in the foetal period, the organs, with the exception of the liver, may be classified as follows:

There are some in which glycogen is constantly present, although in varying quantities, and which are therefore to be regarded as normal deposits of glycogen. To this group belong the voluntary muscles, the myocardium, the lungs, the cartilaginous primordia of the skeleton up to the time when the process of ossification begins, some of the epithelia, particularly the stratified pavement epithelium. In other organs, on the other hand, glycogen is some-

times present and sometimes absent, independently of the degree of their development; in other words, they serve occasionally as depositories of glycogen. These are the pancreas, the salivary glands, the thyroid gland, the parathyroids, the concentric corpuscles of the thymus, the medullary substance of the suprarenal glands, the collecting tubes of the kidneys, the smooth muscles, the genital glands, some of the epithelia, e.g. that of the stomach, larynx, and trachea. And there are still other organs, or parts of organs, which contain glycogen at no period of their development. These are the central nervous system, the cortical substance of the suprarenal glands, the secretory part of the kidneys, the epithelium of the membranous labyrinth, the retina, etc.

With regard to the quantity of glycogen in the various organs during the period of intrauterine life, I have observed that, with the exception of the liver, it begins to diminish in quantity in the first half of the fourth month, this diminution being gradually accentuated, although not in the same degree in the various organs. To be exact, the cartilaginous primordia of the skeleton preserve the quantity of glycogen unaltered up to the time when the process of ossification begins; in the voluntary muscles the reduction is very noticeable; still more so in the myocardium, and extremely so in the lungs. In some parts of the epithelium the quantity diminishes but slightly, disappearing from the stratum of the basal cells only (the epidermis); in others, the diminution is much more noticeable (the epithelium of the oesophagus), and it diminishes to the disappearing point in the epithelium of the larynx and trachea.

At birth, when the glycogenic function of the liver is most active, the organs which constantly conserve glycogen are: first, the voluntary muscles and the myocardium; secondly, some of the epithelia and the lungs.

One last point. In studying the quantity of glycogen in the liver during the period of intrauterine life, decided variations were observed in the quantity of glycogen in subjects of the same age. Now, analogous variations in quantity, which are individual and altogether independent of the degree of development, have been observed in other organs which always contain glycogen during intrauterine life. Of these variations and my views regarding their significance I propose to treat on another occasion.

(32) Monsieur L. ELAUT read a paper on "The suprarenal and insulin," an investigation he had carried out under the direction of Professor GOORMAGHTIGH.

During the preconvulsive period when, as has been proved by experiment, there is an increased output of adrenalin, the cytological features of the medulla are the following: increase in size of nuclei (chiefly juxtacortical); swelling of acidophile nucleoli (dog); mitoses (mouse, dog, rabbit); amitosis (dog); turgescence of cells; turgescence of intracellular network, as shown by Regaud technique and to be considered partly as chondriomes; enlargement of Felicine drainage canals; slight decrease of chromaffinity which, according to previous observations and recent personal research with strychnine (Stewart a. Rogoff) shows a small deficit in the storage of proadrenalin in spite of the above-mentioned signs of activity. When the first fits occur the excretory systems reach a climax, at least quantitatively. Soon after, however, the gland appears to be depleted (no vacuoles, granular chondriomes, etc.). In the dying animal certain zones of the medulla recover (giant nuclei). Very few damaged cells are visible (dog). Regenerative mitoses. A marked decrease of chromaffinity

(as previously shown by Poll and Kahn). The disappearance of the reaction can be, but is not always complete.

The decrease of chromaffinity is not progressive. These fluctuations suggest an irregular course of activity in the gland. The reaction is sometimes stronger in dying animals than in the middle of the convulsive period. It may be suggested that the loss of chromaffinity results from the falling of body temperature, as in fact the animal dies with a very low temperature. The following experiments are not completely in favour of this: thus a rabbit in which insulin somnifene and electric warming cushion are employed, there are no fits and slight decrease of chromaffin-reaction; in a rabbit treated with insulin, somnifene and cooled (22°) there is a more important decrease of chromaffinity but the reaction is more distinct than in animals injected with insulin only. Convulsions appear to be a great factor in the loss of chromaffinity. *Cortical changes.* Lantern slides show variations of the Smith-Dietrich-stained lipoids which we consider the material used for elaboration of the cortical hormone. Preconvulsive period: a disappearance of lipoids occurs constantly in definite zones of the cortex. Convulsive period: the appearances are very variable; loading and unloading follow each other very closely. Agonal or preagonal period: the normally fat-free zona glomerulosa (rabbit) becomes filled with lipoids, while the deeper zones become free from them. This is preceded by mitotic figures in the zona glomerulosa. At death, the appearance of the cortex is not constant. When fits are prevented by somnifene, the cortical lipoid load is very high, at death functional relationship between cortex and medulla appears probable.

(33) Dr Franklin P. Reagan (London) read a paper on "Certain blood vessels of the early embryos of birds and mammals."

An account of the development of the subintestinal artery and of the shifting drainages of the duct of Cuvier (as presented before L'Association des Anatomistes and the Anatomical Society of Great Britain and Ireland) may be found in abstract on pages 481–2 of the *Journal of Anatomy*, Vol. lx, 1925. Only the development of the branchiothoracic drainage need be considered here.

Entering the cephalic side of the duct of Cuvier in the mammalian embryo of ten somites, is a vein comparable to an early vessel described for birds, by Sabin (1917) as the vein of the somatopleure. This vein, which remains practically uninterpreted in previous accounts, may be called the branchio-thoracic vein. It drains the first two branchial arches. In birds this drainage is permanent. In birds and mammals the branchio-thoracic vein enters the portion of the anterior cardinal vein which has been derived from the primitive duct of Cuvier as a result of the ventro-medial shifting of the entrance of the posterior cardinal into the latter. The derivative of the branchio-thoracic vein in birds has been designated the external jugular vein.

In mammals the drainage of these gill arches is gradually abandoned by the branchio-thoracic vein. At the same time, the drainage of the two visceral arches is conducted into a plexiform system of vessels which enters the anterior cardinal vein, and which receives direct tributaries from the ventral aorta. The new drainage enters into the formation of the facial and the external jugular veins. The mammalian branchio-thoracic vein now receives blood from two sources, the ventral aorta (or bases of the aortic arches) and a delicate plexus of veins in the ventral thoracic wall (membrana reuniens). Its longi-

tudinal tributaries lying in the plane of the sides of the future sternum can be injected with difficulty only. They can, however, be demonstrated at all stages in the developmental history of the circulation in the thoracic wall. They attain their full functional status as the main portions of the internal mammary veins at a late stage in development only. At the time of the first appearance of well-developed internal mammary arteries, vessels hitherto mistaken for internal mammary veins lie lateral to them. As the ribs and intercostal musculature invade the membrana, the internal mammary arteries are carried bodily to their final medial position. They are thus transported from an originally lateral position. There is no evidence that the migration of the arteries involves a progressive selection of more and more medially located pre-existing vascular channels, or the abandonment of the originally lateral one. The venous drainage in relation to the arteries does involve the successive enlargement of pre-existing venous channels more and more medial in position. It would seem then, that the internal mammary veins are among the earliest to appear in the mammalian embryo. This is especially true of their cranial ends. Perhaps the earliest stage showing this portion of them interpreted as such, is that of a 30 mm. pig which was figured by Miss Smith (1909) whose account furnishes a basis for the description of the mammary vessels in the *Manual of Human Embryology* by Keibel and Mall.

(34) Mr H. A. Harris read a paper on "The physiological response to reversal of blood flow in cases of congenital heart disease."

Congenital heart disease with patent ductus arteriosus usually shows a reversal of the direction of blood flow in the ductus. Whereas the blood flows from the pulmonary artery to the aorta viâ the ductus arteriosus in foetal life, blood usually flows from the aorta to the pulmonary artery in post-natal life. Thus a variable amount of oxygenated blood is short-circuited from the aorta to the pulmonary circulation without deoxygenation having taken place at the periphery. This load on the circulation may lead to at least two distinct types of compensation. In the first place, the functional amount of haemoglobin is increased by an increase of the red cells to seven or even ten million per cm., and secondly, the rate of the circulation is speeded up by an increase in the blood volume.

Reversal of blood flow in cases of persistent left superior cava with atypical coronary sinus was discussed.

It was suggested that reversal of blood flow in the neo-natal period may be a means of stimulating the blood forming areas by placing a load on the circulation. The rate of closure of the foetal blood vessels and the extent of reversal of blood flow may be a factor in the ambulatory neo-natal efficiency of the sheep, hare, horse and cow on the one hand, and of the helpless condition of the rabbit, dog, cat and man on the other.

(35) Dr A. Blackhall Morison read a paper on "A case of cardiac malformation with vascular anomalies." This will be published in full in the *Journal of Anatomy*.

(36) Dr Kosinski (Wilno) read a paper on "the cutaneous innervation of the dorsum of the human hand."

The distribution of the cutaneous nerves on the dorsum of the hand is differently described by various authors. My investigations have shown that there is a great variation in the distribution of the cutaneous innervation of

the dorsum of the hand, and the following observations are based on the dissection of 300 human hands.

Five nerves are more or less involved in the innervation of the skin of the dorsum of the hand, namely:

Preaxial area

1. Musculocutaneous, C. 5, in 51·3 per cent.
2. Radial, C. 6, in all the cases except one.

Postaxial area

3. Dorsal cutaneous nerve, C. 7, of forearm in 10 per cent.
4. Dorsal cutaneous branch, C. 8, of ulnar nerve—in all cases except 7.
5. Medial cutaneous nerve of forearm in about 4 per cent.

1. *Musculocutaneous.* In the rabbit the cutaneous branch of this nerve is not developed at all. In the dog and monkey it descends on the thenar eminence, and in the cat it anastomoses with the radial nerve sharing with it the innervation of the radial side of the thumb and the adjacent sides of the two first digits.

In man it supplied the radial side of the thumb in about 4 per cent., and in one case it replaced entirely the absent radial nerve. In more than one-third of the cases it shared in the innervation of the radial side of the thumb by means of the anastomotic branch to the radial nerve (38·3 per cent.). In one-tenth of cases it shared in the innervation of the second and the third digits in conjunction with the radial nerve 9 per cent. In more than 10 per cent. of the cases examined I have observed a more distal distribution extending on to the region of the first or second metacarpal bones of the hand (13 per cent.).

Radial. In mammals it has the most extensive area of distribution reaching in the medial direction, to the radial side of the fourth digit, as occurs in the rabbit and monkey, or even to the radial side of the fifth digit in the dog and the cat. In the cat, mainly in conjunction with the ulnar nerve. In man the increased area of distribution was observed in about half of the cases 45 per cent., like that in the dog and cat in 7·3 per cent., and like that in the rabbit and monkey in 25 per cent. This mode of distribution is regarded by many authors as a typical one. The innervation of the three digits was observed in 12·7 per cent. of cases. The most usual distribution peculiar to man and anthropoids, two and a half digits, was present in nearly one-half of the cases (47 %). It is thus evident that the enlarged area of distribution of the radial nerve 45 per cent. as compared with the so-called normal arrangement, peculiar to man and some anthropoids 47 per cent. is equally frequent and may be regarded as normal. Diminished area of distribution of the radial nerve peculiar to man only occurred in 7·7 per cent. In three cases it was due to the increased area of the musculocutaneous nerve.

Dorsal cutaneous of the forearm. In some mammals described by Zander, the digital branch of this nerve descends on to the dorsum of the digits. The area supplied occupies a position between the area of the radial and ulnar nerves.

Ulnar nerve. Dorsal branch to the hand. The complete absence of this branch is stated to occur in 2·3 per cent cases. The corresponding area is mostly supplied by the medial cutaneous nerve of the forearm either by itself, or in conjunction with the radial nerve, or the dorsal cutaneous of the forearm. The diminished area of distribution peculiar to lower mammals is stated to occur in 43 per cent. of cases. This mode of distribution, like that of the

corresponding enlargement of the area supplied by the radial nerve, is subject to many variations, as follows: like that in the dog in 3·3 per cent., like that in the rabbit and monkeys in nearly 10 per cent. The enlarged distribution peculiar to man only in 7 per cent. (21 cases).

Medial cutaneous nerve of the forearm. The greater development and lower descent of this nerve sharing in the innervation of the dorsum of the hand occurred in 3·7 per cent. (11 cases), and in the innervation of the digits in 1·3 per cent. (4 cases only). This mode of distribution has not hitherto been recorded in mammals. In these cases it usually replaced the absent dorsal branch of the ulnar nerve, in 7 cases, 2·4 per cent.

On the dorsum of the hand the most proximal part is mainly innervated by the branches of the ulnar nerve, namely, in about one-half (45·3 per cent.) of cases and in a fourth (28·7 per cent.) of cases by the radial nerve only. With few exceptions no variation attributable to any influence of sex was observed.

In the innervation of the digits in mammals all the collateral branches reached without exception to the ungual phalanx. In man this was the case only as regards the first in which it always occurred, and in the fifth digit in which it very often occurred. On the remaining fingers, especially that of the third digit, the dorsal nerves very often did not extend beyond the base of the proximal phalanx.

No variation in the distribution of the nerves on the palm of the hand in man and mammals was observed.

(37) Dr A. B. Appleton (Cambridge) read a paper on "The phylogeny of the sacrotuberous ligament and of certain mammalian thigh muscles."

The sacrotuberous ligament has originated independently in various mammals and this has not always occurred in the same way. In certain primates its formation was associated with an extension of the origin of the glutaeus maximus muscle to the tuber ischii. Reduction of the hinder part of this muscle in man is referred to the altered mechanical conditions of a greatly extended hip-joint.

The hamstring musculature of Amniota differs from that of Amphibia in the presence of a dorsal as well as a ventral head of origin. This was formed by a dorsal extension across the lateral aspect of the great caudo-femoral retractor muscle. The dorsal head is usually vestigial in mammals but is large in Monotremata in which it has been commonly mistaken for a glutaeus maximus.

The planes of cleavage in hamstring musculature have undergone characteristic modification in the evolution of mammals. One specialised derivative thereof is the mammalian *M. biceps cruris.*

(38) Professor E. J. R. Evatt read a paper on "The nutrient foramina of the longer bones."

During the period of its ossification the diaphysis of each of the longer bones (humerus, radius, ulna, femur, tibia, fibula and the clavicle) has two nutrient arteries, and corresponding nutrient foramina.

The diaphysis of each of these bones has two ossific centres which at first lie in contact with each other, but with the development of the bone separate from each other to accompany the ossifying centres towards the corresponding ends of the bone.

During the whole period of the development of the bone, the relative

positions of the foramina to each other and to the ends of the bone remain constant.

In many of the fully ossified bones a trace of the second nutrient foramen may usually be found.

These bones assume their characteristic form very early in development, and practically no subsequent change of shape takes place. The paper will be published in the *Journal of Anatomy*.

(39) A paper was read for Dr A. TAVARES (Oporto) on "The sub-jugular foramen of Serrano."

The author drew attention to an anomaly which he considers very rare, consisting of a foramen on the jugular surface of the occipital bone, corresponding endocranially to the region of the groove for the termination of the transverse sinus.

Of 586 occipital bones examined, only one showed this variation, to which Serrano gave the name of *Sub-jugular foramen*, and was of the opinion that in the fresh bone it was covered by the external periosteum.

In the case described the aforesaid foramen probably gave passage to a vessel, presumably a vein.

(40) Professor TURCHINI (Montpelier) read a paper on "Differences in potential in histology."

Attention was drawn to the interest presented by the measure of differences in potential, according to the method of Pech (*Bull. de la Société des Sciences médicales et biol. de Montpellier et du Languedoc méditerranéen*, VIII, 1927), between different organs and the blood.

In the Cobaye, differences in potential relative to the blood are always greater in active glandular organs (liver, pancreas, kidneys) than in those where exchanges with the internal medium are less active. The difference in potential between the hemispheres of the brain and the blood, or the contents of the stomach and the blood, is of a sign contrary to that of the differences in the preceding potentials, and give in millivolts the result of the measurements.

He was of the opinion that a similar technique, permitting measurement in other situations of the differences in potential between the tissues and the histological fixing fluids may be used to appreciate the value of the fixing fluids upon a given organ.

(41) Dr JOSEPH (Montpellier) read a paper on "The histological localisation of certain medicaments by their fluorescence in ultra-para violet light."

An endeavour was made to localise certain medicinal substances by their special fluorescence in ultra-para violet light. By means of the methods of Turchini, Carnot and Coquoin, he had observed that sodium salicylate can be localised in articulations and more particularly in cartilage, and that the salts of quinine can be localised chiefly in the spleen which becomes fluorescent by Wood's light, especially when the medium is acidified by acetic acid rather than by the halogen acids. Results of new observations on the localisation of two new extremely fluorescent medicinal substances, esculine and hydrastinine were shown. Esculine was found on the walls of blood vessels, and hydrastinine has a particular affinity for nerve centres and muscles. Thus the examination by ultra-para violet light permits the localisation in a very simple fashion of certain medicinal substances, and the identification of the organs upon which they act.

(42) A paper was read for Professor C. Bressou (Alfort) on "The maintenance of the metacarpo-phalangeal angle of *Tapirus indicus*."

In four-footed animals the interosseous muscles are only developed on the posterior aspect of the metacarpal bones. Their rôle is to maintain the angle of the metacarpus and the digits.

In ruminants and solipedes, these muscles, in order to act more efficiently, are converted into a fibrous band: the suspensory ligament.

Tapirus presents a transitional type. The interosseous muscle is rendered bipenniform by a strong elastic band which is inserted into the sesamoid of the corresponding metacarpal. Another band of the same nature, but smaller, attaches the perforans to the second phalanx.

(43) Dr Payling Wright read a paper on "The oxygen tension necessary for mitosis in chick myoblasts."

Experiments were carried out to determine the lowest oxygen tension necessary for the mitosis of chick myoblasts derived from 12-day-old embryos. The cultures were prepared in small glass tubes through which gas mixtures containing variable quantities of oxygen were passed. At the conclusion of the passage of gas, the culture tube was rapidly sealed at both ends, and a sample of the mixture also collected for gas analysis. The medium employed was a mixture of chicken plasma, saline solution containing glucose and bicarbonate, and a little embryo juice. In order to maintain the necessary hydrogen ion concentration, 3–4 per cent. of carbon dioxide was added to the gas mixture.

The experiments showed that while migration of cells from the original implant took place at oxygen tensions as low as 0·3 per cent. of an atmosphere, mitosis was never found below 6 per cent. of an atmosphere.

DEMONSTATIONS

(1) Professor BRYCE and Professor TEACHER (Glasgow) gave a microscopic demonstration of early human embryos.

(2) Professor LUDWIG (Basle) demonstrated a human embryo showing one pair of somites and a neurenteric canal.

(3) Professor J. P. HILL and Miss C. J. HILL (London): An early Blastocyst of *Hapale.*

Hapale jacchus normally produces twin young. Observations on the late pregnant uterus have shown that each of the twin-foetuses is provided with its own discoidal placenta but the placental vessels of the two are connected by definite anastomoses, whilst the foetuses are enclosed in a common chorion. Study of an early pregnant uterus and the related ovaries has provided the probable explanation of the above conditions. Each ovary showed a prominent corpus luteum, pointing to the probability of the twins being biovular. In the uterine lumen, however, there was present, attached to the dorsal and ventral walls, a thin-walled vesicle, suggestive of a single blastocyst. Examination of this revealed the fact that it contained two embryonal formations, attached at opposite poles of the latter and consisting each of an amnio-embryonal vesicle and an underlying yolk-sac vesicle. Moreover, from the attached ventral and dorsal walls of the vesicle there project inwards two low folds, situated about mid-way between the lateral walls. Our interpretation is that two blastocysts are formed which settle down side by side in the uterus and become attached to the mucosa over their dorsal and ventral polar areas. The apposed walls then proceed to fuse and the conjoint membrane eventually breaks down, the above-mentioned folds representing its last remnants. In this way the two embryonal formations come to be enclosed in a common membrane, destined to form the common chorion. If this interpretation is correct, the trophoblast of each discoidal placental area is composite and really derived from two originally distinct blastocysts.

(4) Miss C. J. HILL demonstrated microscopic preparations showing the enteric plexuses.

(5) Professor TUMA (Prague) exhibited specimens showing interstitial cells of the mammary gland.

(6) Professor LAGUESSE (Lille) showed specimens illustrating the microscopic structure of the umbilical cord in different stages of its development.

(7) Professor DE CASTRO (Madrid). Demonstration of the degeneration and regeneration of pre- and post-ganglionic nerve fibres of the autonomic system.

(8) Professor DEBEYRE (Lille) showed a model, reconstructed in wax, of the mesonephros of a young human embryo.

(9) Professor WILSON (Cambridge). Demonstration of maternal haemopoiesis in the placenta of the rat.

(10) Professor ARON (Strasbourg). Specimens illustrating growth and regeneration in tadpoles.

(11) Professor BENOIT (Strasbourg). Demonstration of a case showing the evolution after ovariotomy, of the rudimentary right ovary of a hen into a sperm-bearing testis, and a specimen of testicular transformation of the parenchyma of the left ovary following subtotal ovariectomy.

(12) Professor DALCQ (Brussels). Fertilisation of the frog's egg.

(13) Dr MACLAREN (Glasgow) gave a demonstration of some early stages in the development of *Cavia*.

(14) J. THORNTON CARTER (London) exhibited a series of photo-micrographs showing the development of the enamel in fishes, marsupials and placental mammals, and demonstrating the fact that the enamel, in all cases, is produced by colloidal changes in the ameloblastic secretion.

The demonstration included a large collection of photo-micrographs of sections of the enamel in a number of mammals, recent and extinct, including the multituberculates, the reptilia, labyrinthodonts and fishes, forming a phylogenetic sequence, to demonstrate the value of enamel structure as a test of affinity.

(15) Professor J. P. HILL (London) exhibited a series of drawings illustrating primate placentation, and the development of monotremes and marsupials.

(16) Professor PARAT and Miss HOPE HIBBARD (Paris). Demonstration of ovogenesis and spermatogenesis in teleosteans.

(17) Professor PARAT (Paris). Behaviour of the vacuome in spermatogenesis.

(18) Professor GATENBY (Dublin). Origin of spermatozoa in *Grantia*.

(19) Mr R. J. LUDFORD (London). The cytology of secretion.

(20) Dr A. S. PARKES, F. W. R. BRAMWELL and UNA FIELDING. Specimens showing the effect of X-rays on the ovary of the mouse; and regeneration of the ovary after double ovariotomy.

(21) Professor CELESTINO DA COSTA (Lisbon). Demonstration of the cranial ganglionic crest in mammals.

(22) Dr R. M. MAY (Paris). Transplantations of the eye and olfactory organ in anuran embryos.

(23) Professor E. P. STIBBE. A comparison of the heads of certain modern South African Tribes.

Summary.

Eight tribes are compared, and it is found that they divide themselves into two groups according to breadth of head and cephalic index; this grouping corresponds to their cultural grouping.

Demonstration.

(1) Tables of length, breadth and height, and of cephalic index, with standard deviations and probable errors.

(2) Tables of comparisons of the data for the different tribes.

(3) Photographs of individuals, with a brief statement of their cultural grouping, which corresponds to the cephalometric classification.

(24) Dr R. Lockhart (Aberdeen) exhibited:

(A) Model of the larynx.

The cartilages, membranes and muscles of the larynx and the hyoid bone have been designed on a large scale, the magnification being about five diameters, each structure is detachable, so that the whole region, sometimes regarded by the student as obscure and difficult, may be built up, piece by piece.

One point observed in the necessary preliminary dissections was the evident continuity of the quadrangular elastic membrane of the larynx down the inside of the cricoid ring to the trachea.

(B) Model of the mid-cranial fossa and related structures.

This model comprises twenty pieces including sheets of dura mater, Meckel's cave, sphenoid and temporal bones, arteries, sinuses and nerves, each one a separate structure. The magnification is fully three times linear, and the model may be dismantled and reconstructed at will, to facilitate the teaching of the detailed anatomy of the region.

Particular care has been observed to demonstrate clearly that the dura of the middle fossa overlies and is adherent to the lateral wall of Meckel's cave, and that the cave extends and forms fully half the height of the lateral wall of the cavernous sinus.

The practical application of these anatomical relations is that the surgeon, instead of approaching the ganglion and roots by burrowing under the dura of the middle fossa, thereby encountering the middle meningeal vessels, may avoid these difficulties by an intradural approach, beneath the temporal lobe; and by an incision through the fused layers of the dura of the middle fossa and the lateral wall of Meckel's cave, may expose the ganglion and roots in their little pocket or glove, in which they appear clean and clear of the fibrous strands, which confuse his decision when the present burrowing method is employed.

(C) Congenital absence of the gall bladder.

The liver showing this variation was removed from a woman of 24 years who died of lung abscess.

There is a little pouch in the wall of the common bile duct suggestive of an arrested attempt to produce the gall bladder in the normal position. The bile ducts dissected into the substance of the liver showed no further sacculation.

The under surface of the right lobe of the liver showed a small peaked lobe near the anterior border, and also a deep transverse fissure running from left to right suggestive of a similar fissure in the lower monkeys. There was a rather large downwardly projecting Spigelian lobe.

The subject showed none of the congenital variations such as cleft palate, cystic kidney, absence of thumb, imperforate anus, etc., which have been seen in association with absence of the gall bladder.

(25) Professor Watrin and Professor Florentin (Nancy). The influence of X-rays on the salivary glands of *Cavia*.

(26) Professor E. Fawcett, Miss Llewelyn and Mrs Dobson (Bristol) exhibited models of the primordial crania of *Myotus schisticolor*, *Galago*,

Mus decumanus, *Homo* and *Hyrax procavia*, and of the laryngo-tracheal skeleton of nycteris.

(27) Professor BELLOCQ (Strasbourg). The temporal bone of the cat.

(28) Professor JULIAN S. HUXLEY and Miss M. A. TAZELAAR exhibited specimens showing modifications of development produced by temperature gradients in frog and chick embryos, and the apparatus employed.

Developing frogs' eggs may be kept, under light compression, between two chambers through which water circulates. By sending hot water through one chamber and cold through the other, two opposed portions of the egg surface may be made to differ in temperature, probably by well over 5° C. So far, experiments have been made only with the temperature gradient running between the two poles of the egg. When the animal pole is heated and the vegetative pole cooled, the temperature gradient may be styled "adjuvant" to the egg's own apicobasal gradient; when the temperature gradient runs in the opposite direction, it is "antagonistic" to the egg's gradient.

When freshly fertilised eggs are exposed to the gradient for 10–20 hours, the effects are as follows: with adjuvant gradient, the difference between the size of animal and vegetative blastomeres is enormously increased; with antagonistic gradient the smallest blastomeres are just above the equator and their diameter may be only half or less that of the cells at the extreme animal pole, whose size in turn is much less different from that of the yolk cells. If the animals are reared to hatching, it is found that adjuvant gradients produce a relatively large head and small body, especially in the belly region (yolk mass). The reverse changes are produced by antagonistic gradients, the animals often having subnormal heads and enlarged abdominal regions. Exposure to an adjuvant gradient prior to, or during early gastrulation may produce a folding of the blastopore lip, which in surface view simulates a double blastopore.

A modification of the method was employed with chicks. Rubber tubes were substituted for the chambers and the eggs carefully adjusted between them. Exposure was usually for the 2 or 3 *first* days of incubation and thus affected growth rather than segmentation or differentiation. Very large increases in the relative size of the heated regions of the blastoderm can thus be produced. In addition, side to side gradients may produce larger limbs and general body-convexity on the heated side. They frequently induce a remarkable forward shift of the mesoblastic somites on the heated side, to the extent of about half a somite. "Adjuvant antero-posterior" gradients produced relatively large heads with abnormal curvatures: antagonistic gradients produce small heads and enlargement and precocious development of the posterior region.

The method is of some theoretical interest, since no part of the egg, in the case of the frog, is exposed to an abnormal stimulus. The only abnormality consists in the alteration of the normal relative rates of development of the various regions.

(29) Dr G. S. SANSOM.

(1) A series of photomicrographs of the placenta of the rabbit to show the origin of placental giant cells.

During the sixth day of gestation, a number of multinucleate trophoblastic thickenings appear on the wall of the still free embryonic vesicle. When the

vesicle becomes attached to the uterine epithelium on the eighth day these trophoblastic masses pass through the epithelium and grow into giant cells.

During the later stages of pregnancy giant cells are proliferated off the trophoblast of the bilaminar omphalopleure into the circum-placental region.

(2) A series of photomicrographs and sections of the early stages of development of the South American bat, Molussus.

(30) Professor GOORMAGHTIGH and Mr L. ELAUT (Gand). Suprarenals and insulin.

(31) Professor GOORMAGHTIGH (Gand). The thyroid in the pregnant bitch. The lutein cells of the bitch.

(32) Mr H. A. HARRIS (London).

(A) Bony striations of the metaphysis as an indication of cessation of growth in long bones.

(B) Radiography in the teaching of anatomy.

(33) Dr L. R. SHORE showed microphotographs illustrating the effects of injecting gelatin masses into the coronary arteries.

It seems that the mitral and tricuspid valves of the heart of sheep and calf contain blood vessels in about one-third or one-half of the cases examined. Vascularisation of the aortic and pulmonary valves has not been demonstrated.

Microphotographs of the lymphatic vessels of the heart, of sheep and rabbit, both sub-endocardial and intra-muscular, were also shown.

(34) Professor J. C. BRASH showed madder specimens illustrating the growth of the skull and jaws. The majority of the specimens were obtained from pigs treated by the "indirect madder method," the animals having been madder-fed from birth and the madder stopped at increasing ages and for suitable periods to demonstrate growth sites by the addition of new unstained bone, and removal of old bone by absorption.

The general mode of growth of the skull was illustrated by a complete skull and mandible of a pig, one year old, showing twelve weeks' growth, and details by sectioned and disarticulated skulls and a series of half-mandibles. The importance of alveolar growth for the general increase in size of the jaws, and in connection with the normal growth movements of the teeth, including their eruption, was illustrated by a series of sections of mandibles and maxillae. The growth movements of the malar process of the maxilla and of the maxillary antrum were demonstrated by sections of maxillae, and specimens were shown to illustrate the mode of enlargement of the cranial cavity, and the growth changes therein consequent on extension of the frontal sinuses.

The chemical basis of the madder method was illustrated by a series of exhibits, including test-tube reactions and skulls of rats and rabbits. These exhibits demonstrated that pure alizarin and pure purpurin are both capable of staining the bone with characteristic colours, but that purpurin is much the more powerful, and that madder, contrary to the general belief, owes its vital staining property not to its alizarin but to its purpurin content.

(35) Dr REAGAN (London) showed drawings and specimens illustrating the development of blood vessels in early embryos of mammals and birds.

(36) Professor J. L. SHELLSHEAR. A contribution to our knowledge of the arterial supply of the cerebral cortex.

The opinion of the writer, shared with Professor Dart, that the sympathetic nervous system is peripheral in origin led to an investigation of the distribution

of the arteries of the brain. In a large series of vertebrate brains, the arterial supply is found to be phylogenetically constant; and this constancy is held to be due to the fact that the sympathetic nervous system is developed with the arteries and structures supplied by those arteries, as a component of the mechanism formed by these structures.

The cortical supply of one Chinese brain, in which the anterior, middle and posterior cerebral arteries were injected, is described. The most striking feature in this brain, confirmed in several Orang brains, is the exactitude of the correspondence between the arterial area of supply of the calcarine branch of the posterior cerebral artery and the cortical area to which the stria of Gennari is limited. The arterial supply confirms the morphological observations of Elliot Smith on the sulcus lunatus, as well as those of the writer on the sulcus named "pars mesialis sulci lunati."

The arterial supply to other areas is likewise dealt with.

(37) Mr V. E. Negus (London). Specimens illustrating the function of the epiglottis.

(38) Dr Blackhall Morison (London). The innervation of the human atrium.

(39) Dr Vonwiller (Zurich) demonstrated a new method for observation of the blood stream on the lower aspect of the tongue in mice. He employed a high magnification (Leitz, Obj. 5–6 *a*, Seibert 6 *a*). Narcosis was induced by the use of somnifene (Hoffmann-Laroche). An injection into the tongue of aluminium powder in oil, served as an artificial reflector. An indirect illumination was obtained by a vertically incident light. A new table was used, which was moved by means of ordinary and micrometric screws. Experiments were also described on the compression of blood vessels by means of a modified micro-manipulator, and the application of this method of microscopy in the observation of the circulation in the capillaries at the edge of the human nail.

(40) Dr Vonwiller and Dr Demole (Zurich). A method of observation of living parasites (trypanosomes) in the blood of living mammals.

(41) Dr J. Morel (Lille). A set of preparations illustrating the development of the vitreous body in the embryo chick, showing *direct continuity with the mesodermal stroma of the cornea and its lamellar structure.*

(1) A transverse complete section of an 82 hours chick-embryo showing persistence of the continuity of the original vitreous body with the mesodermal stroma of the cornea. The vitreous has been delaminated and pushed backwards by the lens.

The removal with a razor of the remaining part of the rim of the lens shows clearly the continuity of the cornea mesostroma (anterior vitreous) with the vitreous mesostroma (posterior vitreous).

(2) A transverse complete section of the eye of a 4½ days chick-embryo, giving a slightly magnified and general view of the vitreous body and displaying its decidedly lamellar structure.

(3) Two sections of the same embryo showing, more magnified, the existence of lamellae in the incipient vitreous body. The tissue is altogether destitute of cells. This peculiar structure of the tissue is, moreover, to be found in many other parts of the preparation. One of the figures displays a part where the vitreous body is still normally connected with the wall of the optic vesicle.

(42) E. A. Fraser. Models of the developing pronephros in *Acipenser rubicundus.*

(43) A. Francis Dixon. A section through a human oöcyte showing the first polar body, and the nucleus of the oöcyte in the metaphase stage of the division which would have resulted in the formation of the second polar body.

The ovary from which the section was taken was removed from a young adult woman at an operation, and fixed while still warm.

The oöcyte was contained in its ovarian follicle and was enclosed in a thick homogeneous oölemma (zona pellucida) which showed no radial or concentric markings. Between the cytoplasm of the oöcyte and the oölemma was a narrow somewhat crescentic perivitelline space partially occupied by the first polar body. The rest of this space was occupied by a very finely granular material. No trace of a vitelline membrane was visible and the cytoplasm itself formed the inner wall of the perivitelline space. Within the cytoplasm, at one place, was a collection of chromosomes each of which was very clearly defined. These chromosomes were so arranged as to show that the section had passed obliquely through the region of the equatorial plate of the dividing nucleus. It is not possible to state the total number of the chromosomes present as the sections immediately following the one exhibited are not perfect.

The specimen supports the view that in the human subject both polar bodies are formed while the oöcyte is still in the ovarian follicle and before fertilisation takes place.

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